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TOTAL SYNTHESIS OF (±)$\Delta^{9(12)}$-CAPNELLENE

BY

M. G. KULKARNI

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A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

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TOTAL SYNTHESIS OF (±)$\Delta^{9(12)}$-CAPNELLENE

submitted by M. G. KULKARNI in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

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Supervisor

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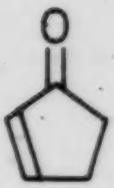
External Examiner

Date May 17, 1985

ABSTRACT

A total synthesis of $\Delta^{9(12)}$-capnellene (XXII) was achieved in a regio- and stereo-selective manner starting from 2-cyclopentenone (I). (2+2) Photocycloaddition of 2-cyclopentenone (I) to 1,1-diethoxyethene furnished the bicyclo[3.2.0]heptanone derivative II which on reduction with lithium tri-t-butoxyalumino hydride gave the alcohol III. Benzylation of this alcohol followed by the hydrolysis of the diethyl ketal moiety with aqueous oxalic acid gave the cyclobutanone IV. The keto-ester V was formed when the cyclobutanone IV was treated with boron trifluoride etherate and ethyl diazoacetate. The treatment of the keto-ester V with sodium hydride and phenylselenenyl chloride followed by the oxidation of the resulting selenide VI with aqueous hydrogen peroxide furnished the enone VII. Stannic chloride catalyzed Diels-Alder reaction of the enone VII with isoprene produced the tricyclic keto-ester VIII. Reduction of this keto-ester VIII with sodium bis[2-methoxyethoxy]aluminium hydride gave the diol IX as a single product. On treating the diol IX with phenyl chlorothionocarbonate and 4-(N,N-dimethylamino)pyridine, the thionocarbonate X was produced which on reduction with tri-n-butylstannane and 2,2'-azobis[2-methyl-2-propionitrile] afforded the monoalcohol XI. The treatment of this monoalcohol with potassium



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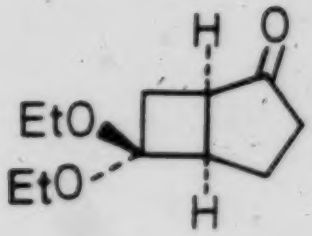

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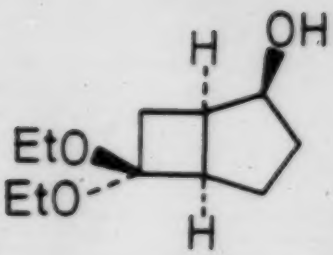

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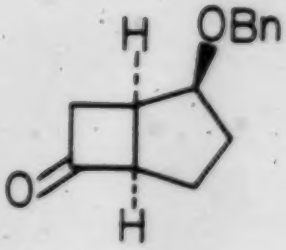

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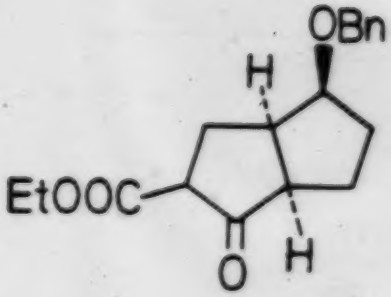

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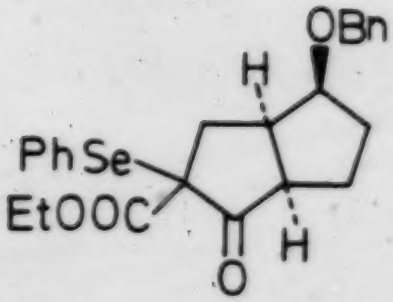

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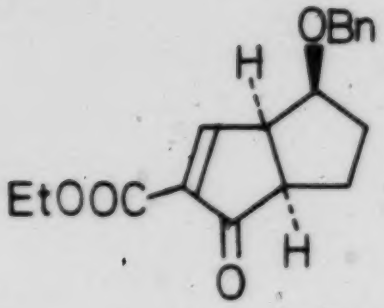

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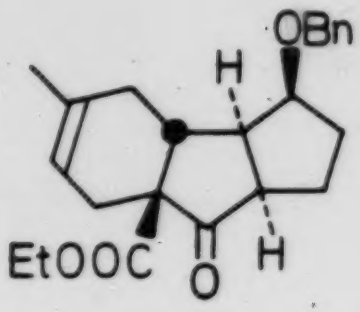

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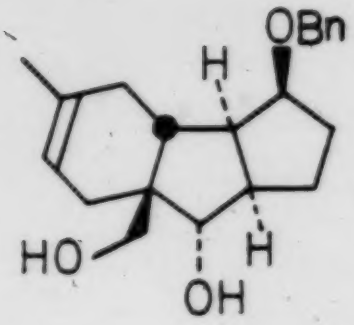

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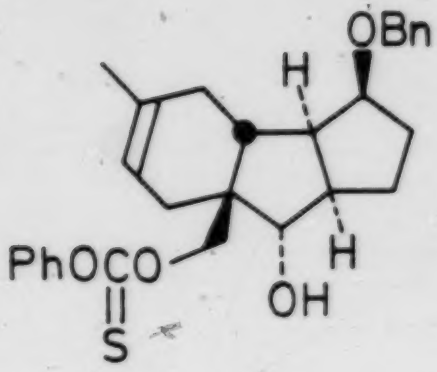

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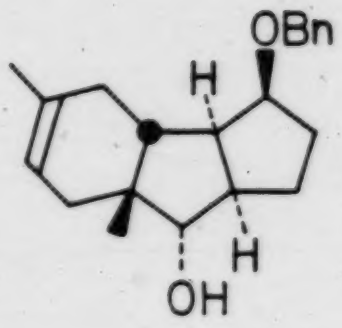

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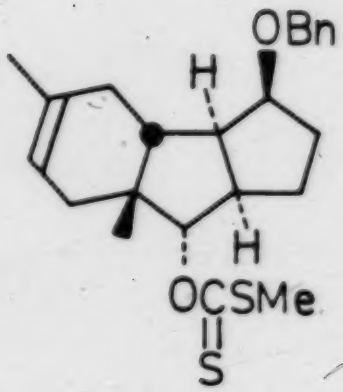
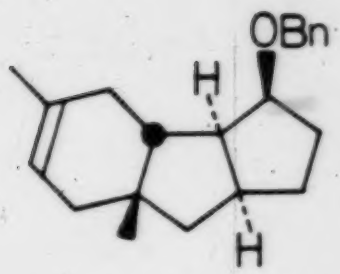


XII

hydride and carbon disulfide followed by the addition of an excess of methyl iodide resulted in the formation of the xanthate XII. Reduction of the xanthate XII with tri-n-butylstannane and 2,2'-azobis[2-methyl-2-propionitrile] furnished the tricyclic compound XIII. Ozonolysis of the compound XIII followed by the reductive workup with dimethyl sulfide directly produced the enone XIV. When treated with phosphorus oxychloride, the oxime XV, prepared from the enone XIV, smoothly underwent the Beckmann rearrangement to furnish the ketone XVI. Wittig reaction of this ketone with methylenetriphenylphosphorane gave the methylidene compound XVII. On hydrogenolysis with 5% palladium on carbon, the cyclopropane XVIII, obtained from the reaction of the olefin XVII with diethylzinc and methylene iodide in the presence of air, gave the alcohol XIX. Hydrogenolysis of this cyclopropyl alcohol XIX with platinum black produced the alcohol XX. The oxidation of this alcohol with pyridinium chlorochromate gave the known ketone XXI which on Wittig reaction with methylenetriphenylphosphorane furnished the naturally occurring triquinanoid sesquiterpene $\Delta^{9(12)}$-capnellene (XXII) in racemic form.



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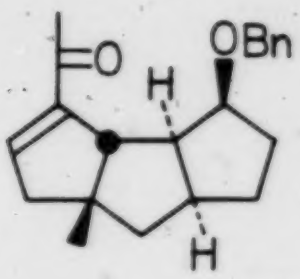

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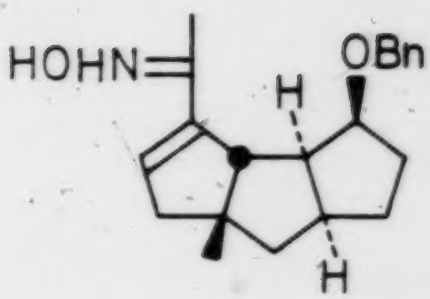

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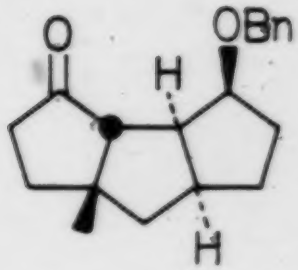

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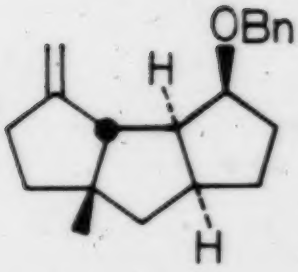

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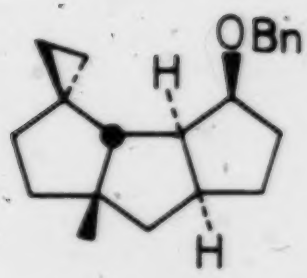

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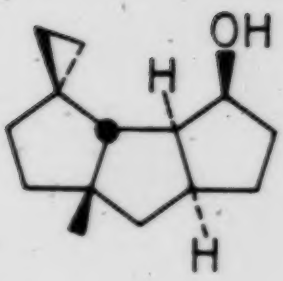

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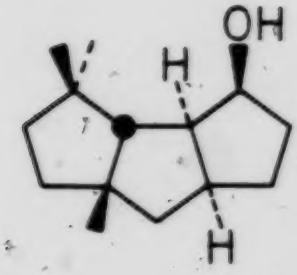

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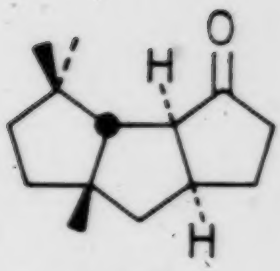

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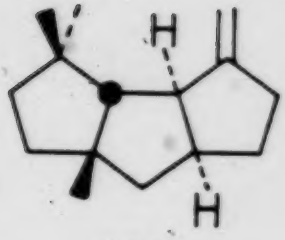

XXII

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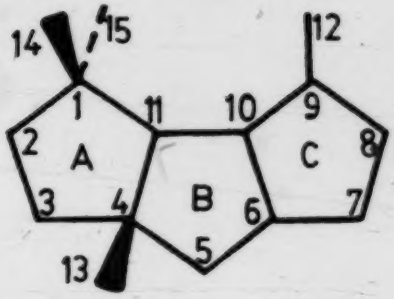
INTRODUCTION

In a series of publications in the mid-seventies, Djerassi and co-workers reported the structure determination of a group of closely related sesquiterpenes isolated from soft coral Capnella imbricata (Quoy and Giamard 1833) indigenous to the Indonesian coastal area. In the first report[1] the structure **4** was established for the most abundant compound by extensive spectroscopic studies, especially the proton and carbon-13 NMR, and by chemical degradations. This structural assignment was further confirmed by single crystal X-ray analysis. This compound was named as $\Delta^{9(12)}$-capnellene-3β,8β,10α-triol on the basis of the trivial name, capnellane, coined for the parent hydrocarbon **1** which represents a new type of triquinanoid[2] sesquiterpene skeleton.[1]

In subsequent publications[3,4] the structures of four other compounds were reported. All of these compounds were shown to be oxygenated capnellenes similar to the triol **4**. A careful comparison of their spectral data with those of triol **4** led to the assignment of structures **3**, **5**, **6** and **7** to the new capnellanoids. These assignments were further confirmed by their chemical correlation with triol **4** and, in the case of **7**, also by a single crystal X-ray analysis.



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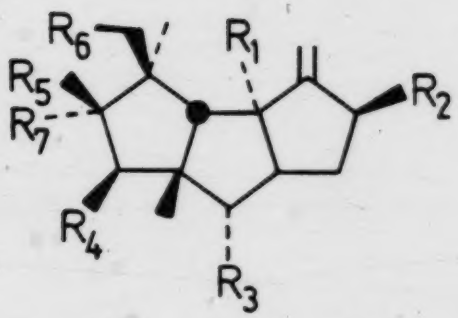


2 $R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_7 = H.$

3 $R_1 = R_2 = OH;\ R_3 = R_4 = R_5 = R_6 = R_7 = H.$

4 $R_1 = R_2 = R_4 = OH;\ R_3 = R_5 = R_6 = R_7 = H.$

5 $R_1 = R_2 = R_3 = OH;\ R_4 = R_5 = R_6 = R_7 = H.$

6 $R_1 = R_2 = OH;\ R_5 = R_7 = H,OH;\ R_3 = R_4 = R_6 = H.$

7 $R_1 = R_2 = R_4 = R_6 = OH;\ R_3 = R_5 = R_7 = H.$

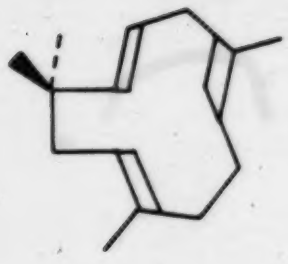
8 $R_1 = R_2 = R_3 = R_5 = OH;\ R_4 = R_6 = R_7 = H.$

In continuation of their work on the metabolites of Capnella imbricata, Djerassi and co-workers[5] isolated a new hydrocarbon from the pentane extract. The proposed structure **2** for this hydrocarbon was based on the detailed examination of its spectral data. This was further confirmed by correlating it with diol **3**.

More recently, Tursch and co-workers[6] reported the isolation of yet another capnellanoid from the same natural source. The compound was found to possess the structure **8** from the indepth spectral investigation of its triacetate derivative. This assignment was later shown to be correct by X-ray analysis.

Although the biosynthetic pathway leading to the capnellanoids remains to be elucidated, it has been suggested[7] that the carbon frame work of capnellanoids is derived from humulene (**9**) by a series of transannular reactions involving precapnelladiene (**10**) as a key intermediate. The co-occurrence of precapnelladiene (**10**) with capnellanoids[7] supported the above biosynthetic proposal.

As far as the biological activity of capnellanoids is concerned, they are a part of the chemical defence system of the animal against predators as indicated by the ability of the animal to ward off the algal and microbial growth and to prevent the settlement of larvae.[3] Furthermore, preliminary screening studies have indicated that



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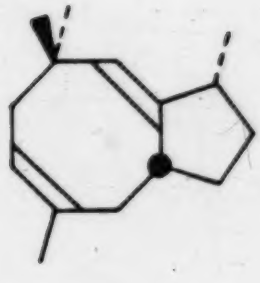

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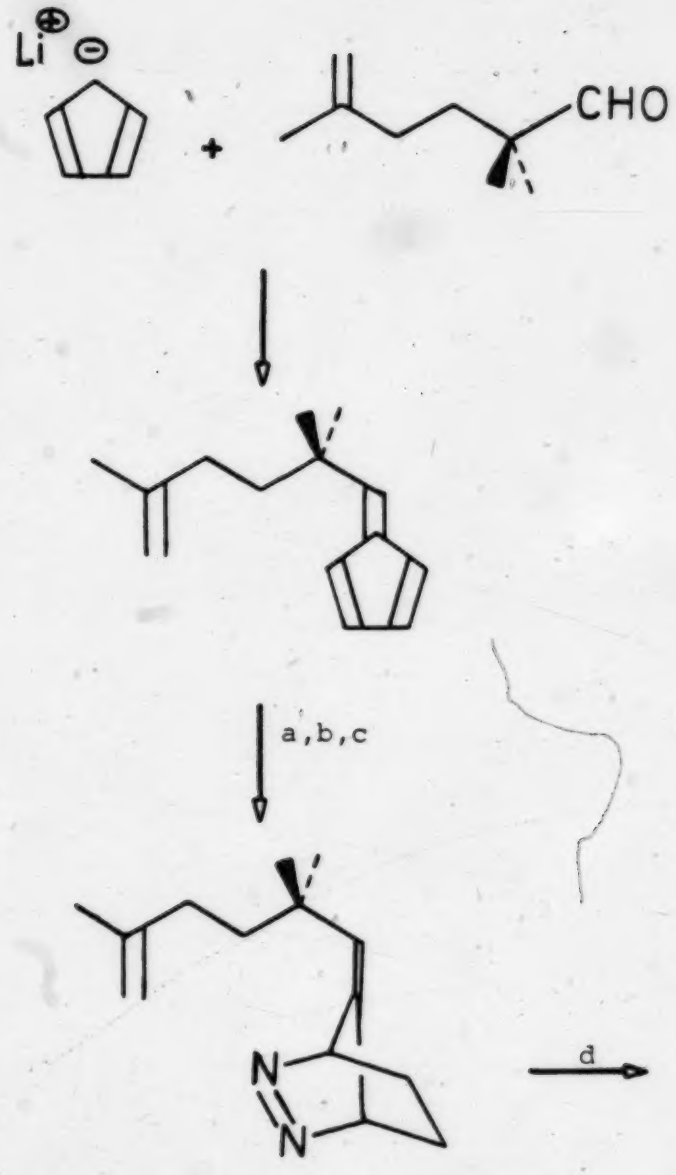
some of the capnellanoids, like triol **4**, may possess useful antibiotic activity.[8]

We were intrigued by the novelty of the capnellane skeleton and the complexity of its congeners, especially the enediol functionality embeded in their structure. Also the fact that capnellanoids may possess useful antibiotic activity further enhanced our interest in devising an approach to their synthesis. As a result, several years ago a project dealing with the synthesis of capnellanoids was initiated. $\Delta^{9(12)}$-Capnellene (**2**), the simplest member of the family, was selected as the initial target. The synthetic scheme was so designed that it could be applied to more complex capnellanoids with slight modifications. At the onset of the present work there were no reports in the literature concerning the synthesis of $\Delta^{9(12)}$-capnellene (**2**). However during the course of present work several reports describing the synthesis of this hydrocarbon have appeared. The first two of the syntheses were simultaneously reported by two independent groups.[9,12a]

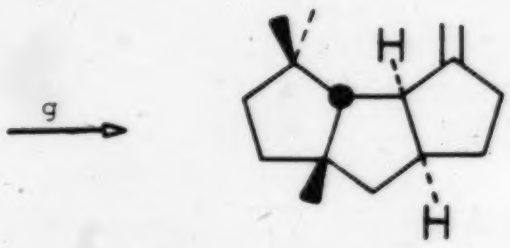
The synthesis by Little and coworkers[9,10,11] employed an intramolecular 1,3-diyl trapping reaction to establish the required triquinane skeleton which was then further elaborated to yield the natural product. Thus, the reaction of 2,2,5-trimethyl-5-hexenal with cyclopenta-

Scheme I



11

12 13



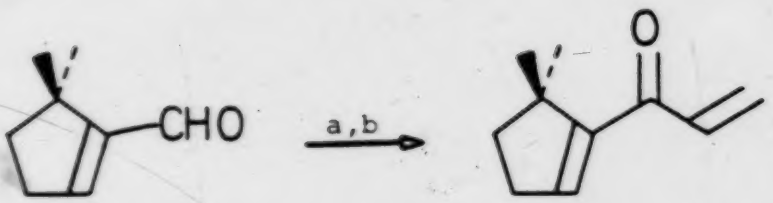
2

a.MeOOC-N=N-COOMe. b.KOOC-N=N-COOK. c.KOH,EtOH,reflux; cool to 0°C;$K_3Fe(CN)_6$. d.THF,heat. e.BH_3.THF;NaOH,H_2O_2. f.PCC,CH_2Cl_2. g.$Ph_3P{=}CH_2$.

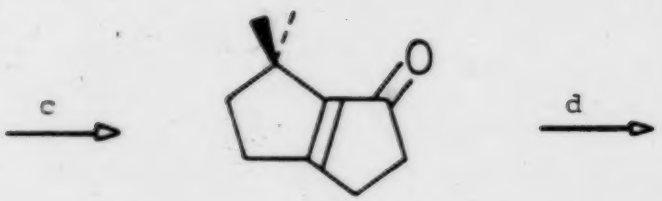
dienyllithium gave the corresponding fulvene derviative (Scheme I). Diels-Alder reaction of this fulvene with dimethyl azodicarboxylate followed by selective hydrogenation, saponification, decarboxylation and oxidation gave the required diyl precursor **11**. Pyrolysis of this compound under carefully controlled conditions[11] gave the compound **12** possessing the required triquinane skeleton, albeit in rather poor yield. Subsequent hydroboration and oxidation of **12** gave the tricyclic ketone **13** in 10% yield over three steps. Wittig reaction of **13** with methylenetriphenylphosphorane gave the required hydrocarbon, (±)-$\Delta^{9(12)}$-capnellene (**2**).

Paquette and co-workers[12a,b] accomplished the synthesis in a rather conventional manner. 5,5-Dimethylcyclopenten-1-yl-carbaldehyde (**14**) was first converted to the divinyl ketone **15** (Scheme II). A Nazarov-type reaction of this ketone resulted in the formation of the bicyclo[3.3.0]octane derivative **16**. After the required C-4 (capnellane numbering) angular methyl group was introduced to the ketone **16**, it was converted to the keto-aldehyde **17** through functional group manipulations. Intramolecular aldol condensation of the keto-aldehyde **17** followed by hydrogenation furnished the ketone **13**. Subsequent introduction of an exo-methylene group using

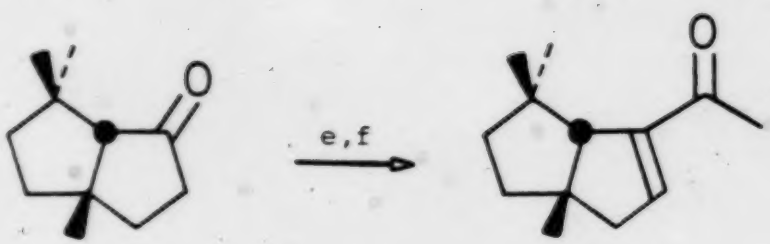
Scheme II

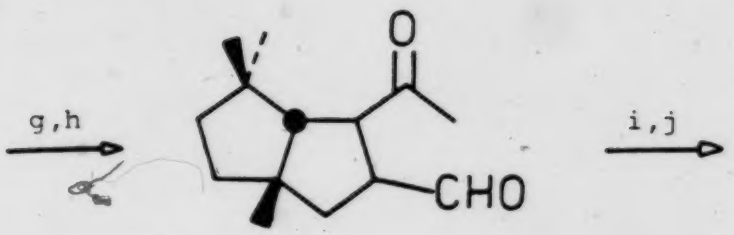


14 15

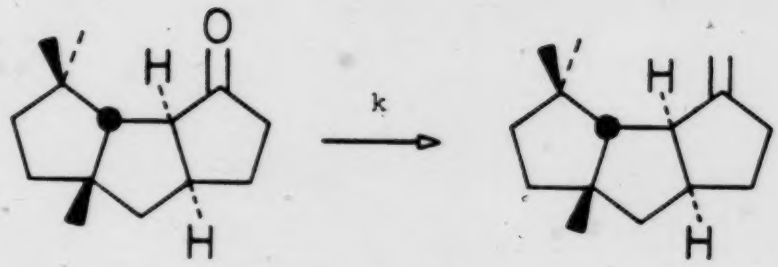


16





17



13 2

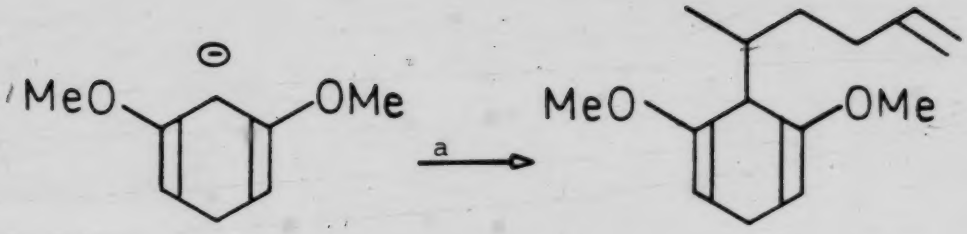
a.CH_2=CHMgBr. b.MnO_2. c.P_2O_5,CH_3SO_3H. d.Me_2CuLi.
e.HC≡CLi. f.HCOOH,H_2SO_4,90°C. g.CH_2=CHMgBr,CuI.
h.O_3;Me_2S;HCOOH. i.KOH,THF. j.H_2Pt,EtOAc. k.CH_2=PPh_3.

Wittig reaction gave the natural product **2** in the racemic form.

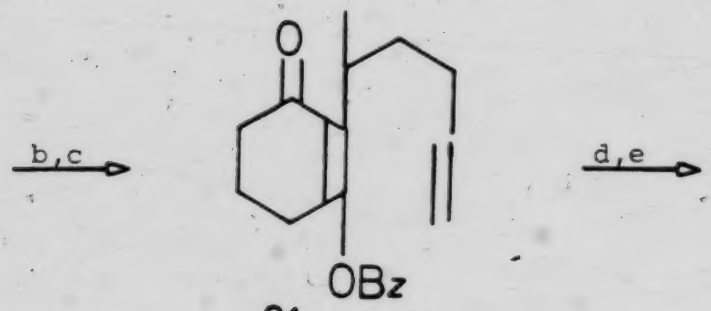
As mentioned earlier, Djerassi and co-workers[6] have proposed that the capnellanoids are biosynthesized from precapnelladiene (**10**). To test this hypothesis Pattenden and co-workers[13] prepared epiprecapnelladiene (**18**) using an intramolecular photocycloaddition-fragmentation reaction sequence as shown in Scheme III. The required starting compound **20** was obtained by alkylation of the anion of 1,5-dimethoxy-1,4-cyclohexadiene (**19**) with 5-iodo-1-hexene. Acid hydrolysis of **20** followed by benzoylation of the resulting 1,3-dione gave the enol-benzoate **21**. Irradiation of this compound followed by exhaustive methylation produced the tricyclic compound **22**. Base-induced fragmentation of this benzoate followed by modification of the existing functionalities led to the formation of epiprecapnelladiene (**18**). On treatment with boron trifluoride etherate, this diene underwent cyclization giving rise to Δ^{8}-capnellene (**23**) as the major product along with small quantities of the regioisomers **24** and **25** (Scheme IV). However the desired isomer **2** was not produced.

In the biomimmetic synthesis of $\Delta^{9(12)}$-capnellane (**2**) by Fujita and co-workers,[15a] the olefin **23** was prepared by a different route and was further elaborated to the

Scheme III

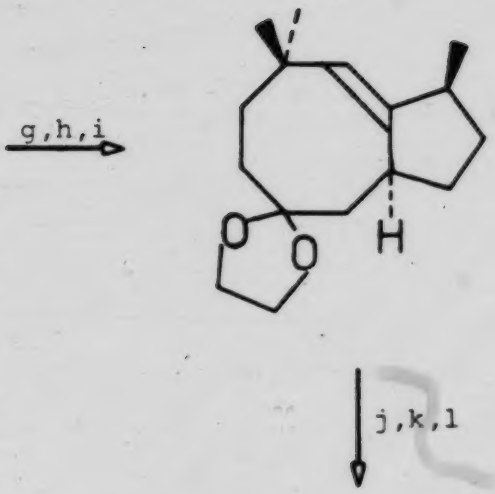


19 20



21

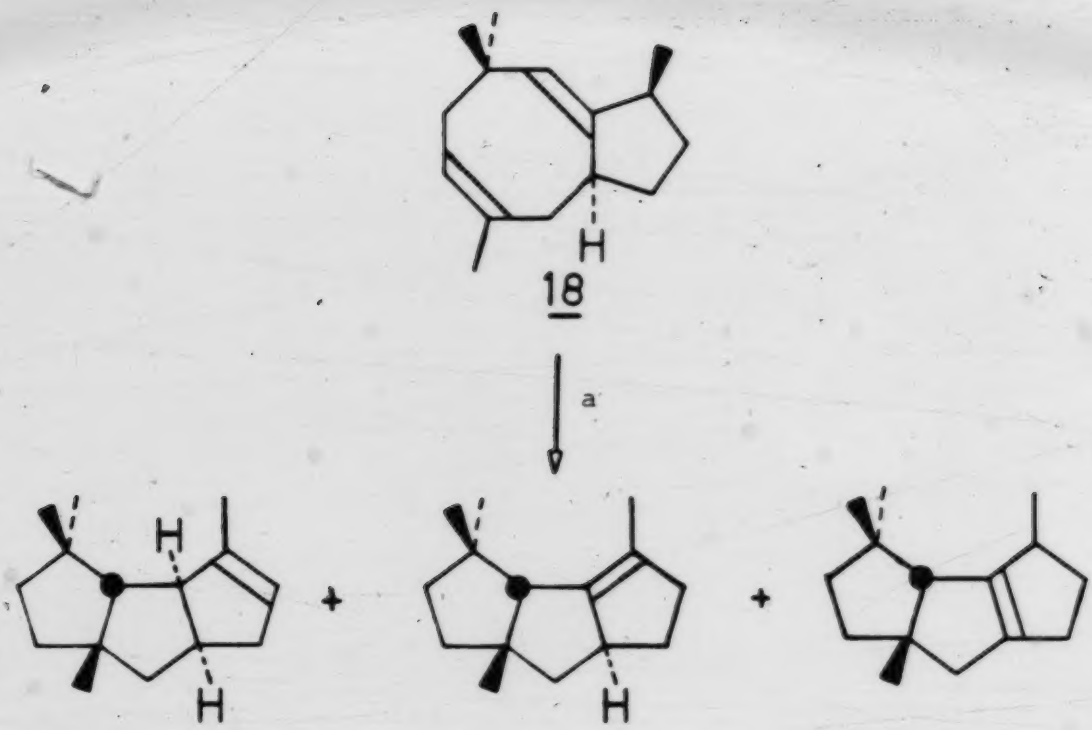
22



18

a.5-iodo-1-hexene,HMPA. b.1M HCl. c.Py,PhCOCl. d.hν. e.$LiN(SiMe_3)_2$,MeI. f.aq.KOH. g.$HOCH_2CH_2OH$,PhH,PTSA. h.LAH. i.Py,$POCl_3$. j.THF-H_2O-AcOH. k.CH_2=PPh_3,THF. l.EtOH,$RhCl_3$, reflux.

Scheme IV

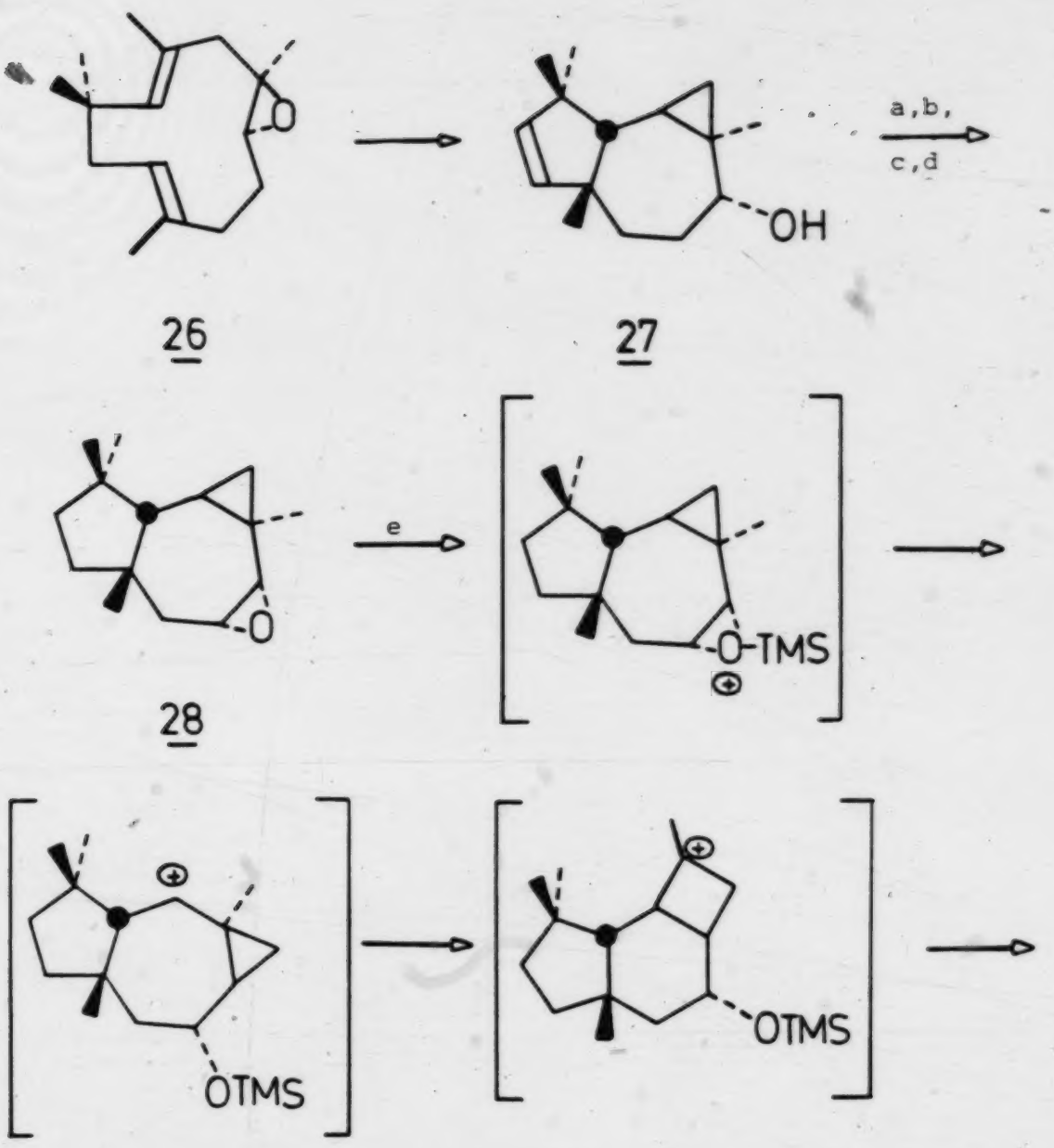


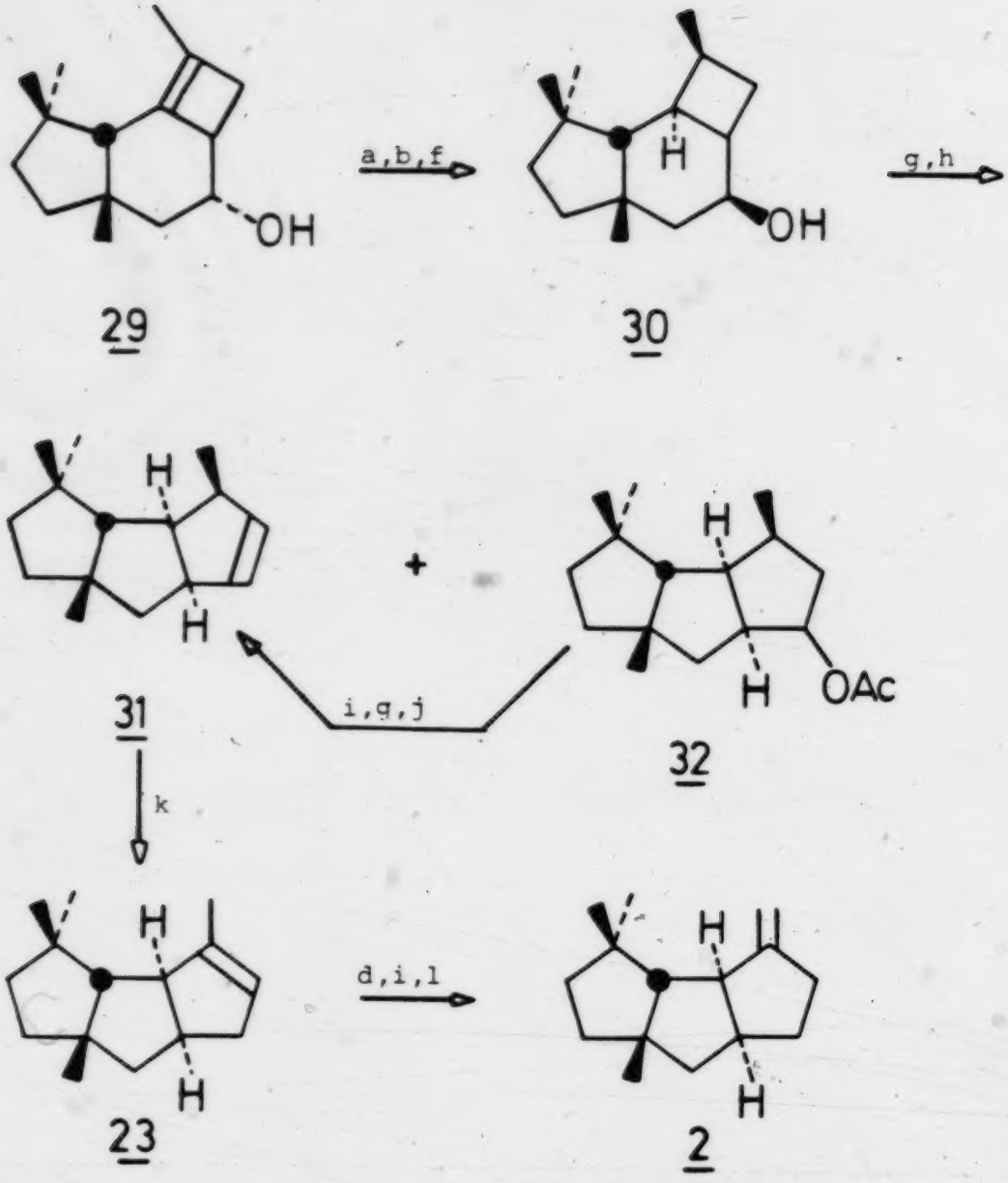
a. $BF_3.Et_2O$, PhH, reflux.

natural product (Scheme V). Thus, humulene-6,7-epoxide (**26**) was converted to the alcohol **27** following the reported procedure.[15b] By a series of functional group transformations the alcohol **27** was converted to the tricyclic epoxide **28** (Scheme V). Trimethylsilyl triflate mediated rearrangement of this epoxide gave a mixture of three compounds. The major compound was characterized as the alcohol **29** on the basis of an extensive study of its spectral data. The formation of the alcohol **29** requires the migration of the angular methyl group which can be rationalized by a cyclopropane sliding mechanism as shown in the Scheme. Hydrogenation followed by inversion of the stereochemistry of the hydroxy group gave the compound **30**. Acetolysis of the corresponding mesylate resulted in the formation of the olefin **31** along with the acetate **32** which was modified to provide an additional quantity of the olefin **31**. Isomerization of this olefin with rhodium trichloride produced the compound **23**, the endo-cyclic double-bond of which was eventually transposed to the exo-cyclic position through a three step reaction sequence to obtain $\Delta^{9(12)}$-capnellene (**2**).

Using α-alkynone cyclization in an iterative way, Dreiding and co-workers[16] also succeeded in synthesizing $\Delta^{9(12)}$-capnellene (**2**) (Scheme VI). Exhaustive methylation of methyl 2-oxocyclopentanecarboxylate (**33**).

Scheme V



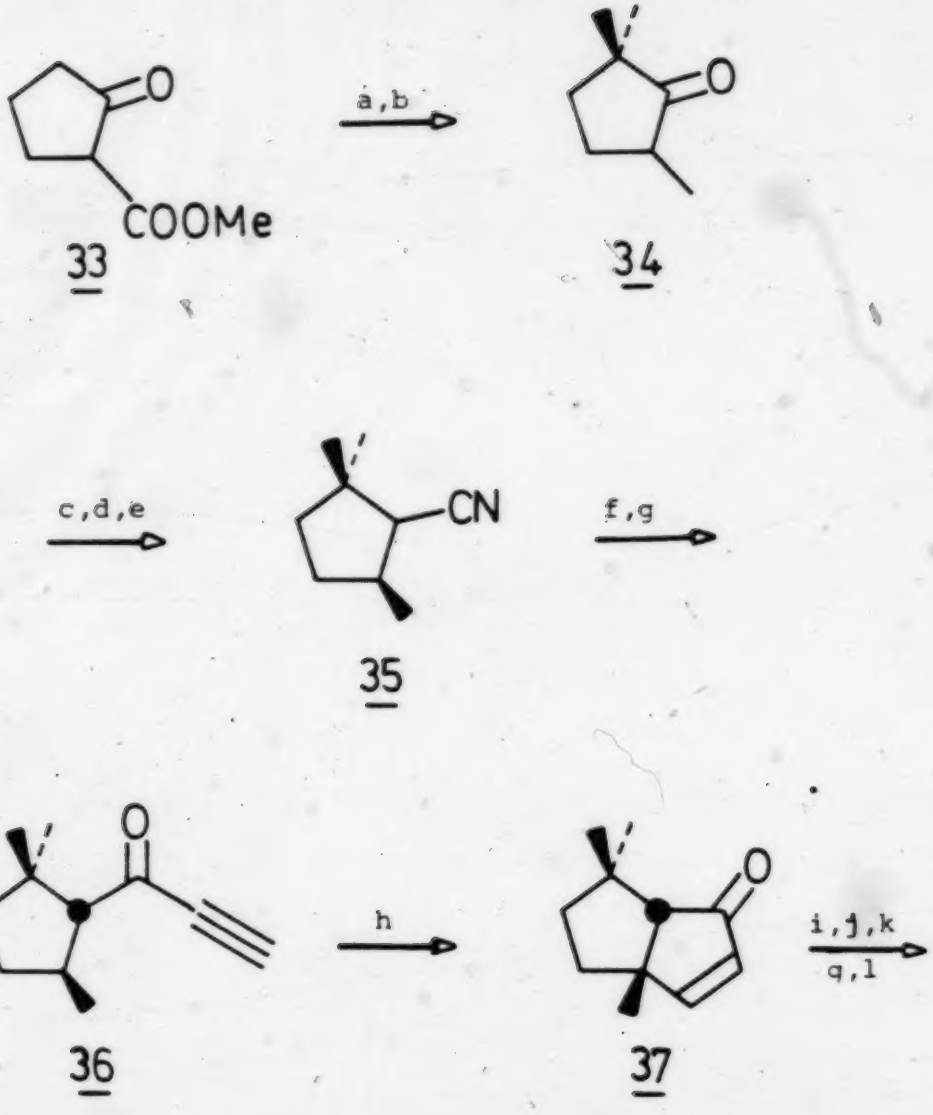


a.H_2,Pt,EtOAc. b.Jones reagent. c.$TsNHNH_2$,PTSA,n-BuLi. d.MCPBA. e.Me_3SiOTf. f.L-selectride. g.MsCl,DMAP. h.AcOH, NaOAc,80°C. i.LAH. j.basic Al_2O_3, k.$RhCl_3$,EtOH,reflux. l.$CF_3CHFCF_2NEt_2$ - $CF_3CF{=}CFNEt_2$(1:1),THF,reflux.

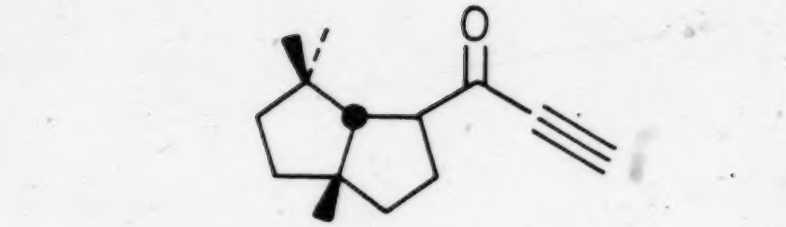
followed by decarbomethoxylation gave 2,2,5-trimethylcyclopentanone (**34**). Cyanohydrin formation of the ketone **34** followed by dehydration and hydrogenation produced the nitrile **35** which was then converted to the α-alkynone **36**, required for the cyclization reaction. Vacuum pyrolysis of **36** gave a good yield of bicyclo[3.3.0]octane derivative **37**, possessing the A/B ring system of the capnellane skeleton **1**. Through a series of steps **37** was transformed into another α-alkynone **38** which, on vacuum pyrolysis as before, underwent cyclization giving the tricyclic enones **39** and **40** in approximately equal quantities. Subsequent hydrogenation of **39** gave the known tricyclic ketone **13** which was converted to the natural product **2** by the Wittig reaction.

Iterative use of intramolecular "magnesium-ene" reaction by Oppolzer *et al.*[17] resulted in a new synthesis of $\Delta^{9(12)}$-capnellene (**2**) (Scheme VII). The allylic chloride **42**, prepared from aldehyde **41**, was treated with magnesium metal. The resulting Grignard reagent on heating at 60°C underwent the "magnesium-ene" rearrangement. The rearranged Grignard reagent thus produced was trapped with acrolein to give the alcohol **43** which was then converted to the allylic chloride **44**. A second "magnesium-ene" rearrangement of the corresponding allylic Grignard reagent followed by treatment with oxygen

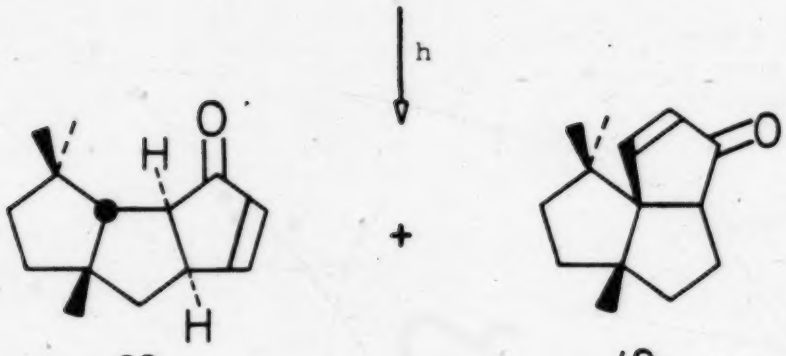
Scheme VI



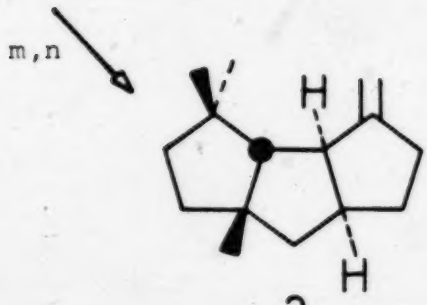
33 34 35 36 37



38



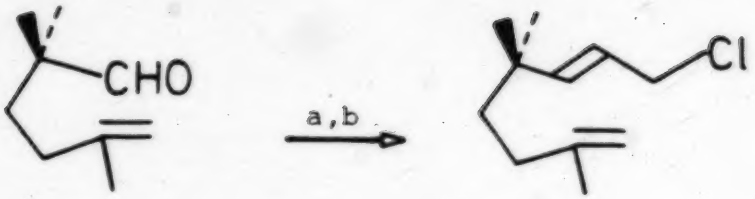
39 + 40



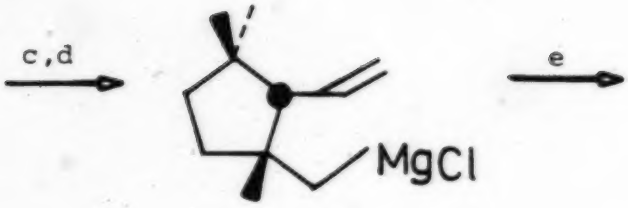
2

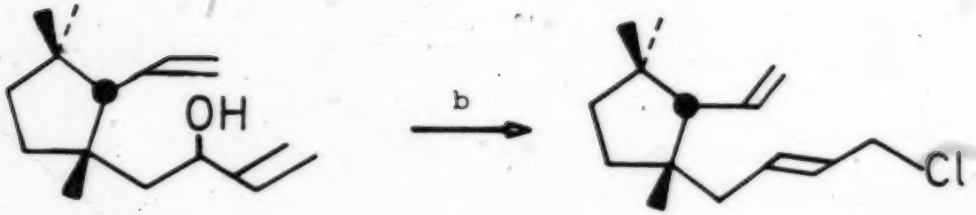
a.MeI(excess),NaH. b.KOH,MeOH;HCl,heat. c.TMSCN;F^-. d.Py,$POCl_3$. e.CuH complex. f.KOH,diglyme. g.$SOCl_2$;TMS-C≡C-TMS;F^-. h.vacuum pyrolysis. i.H_2,Pd-C,EtOH. j.$MeOCH{=}PPh_3$, THF. k.10%HCl. l.Jones reagent. m.H_2,Pt,EtOAc. n.$CH_2{=}PPh_3$,THF.

Scheme VII

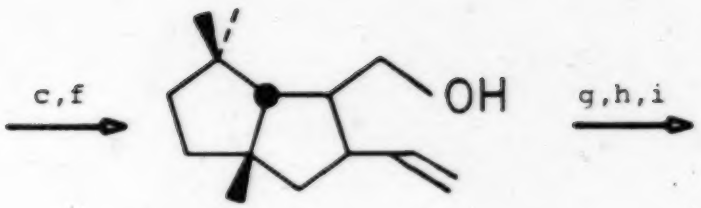


41 42





43 44



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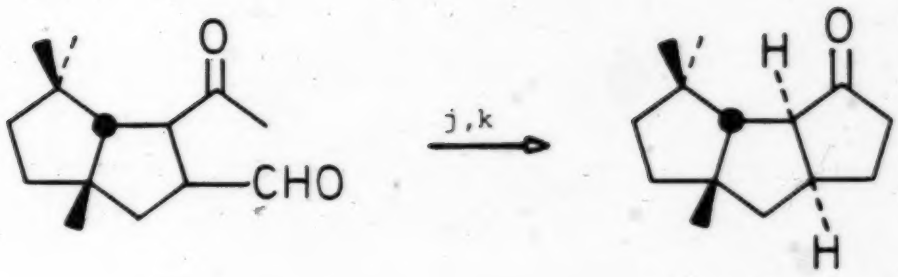
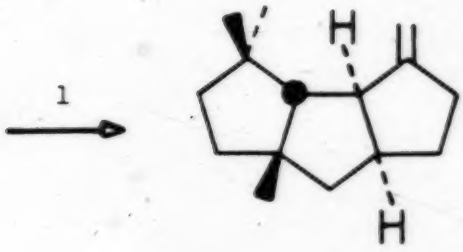


17 13



2

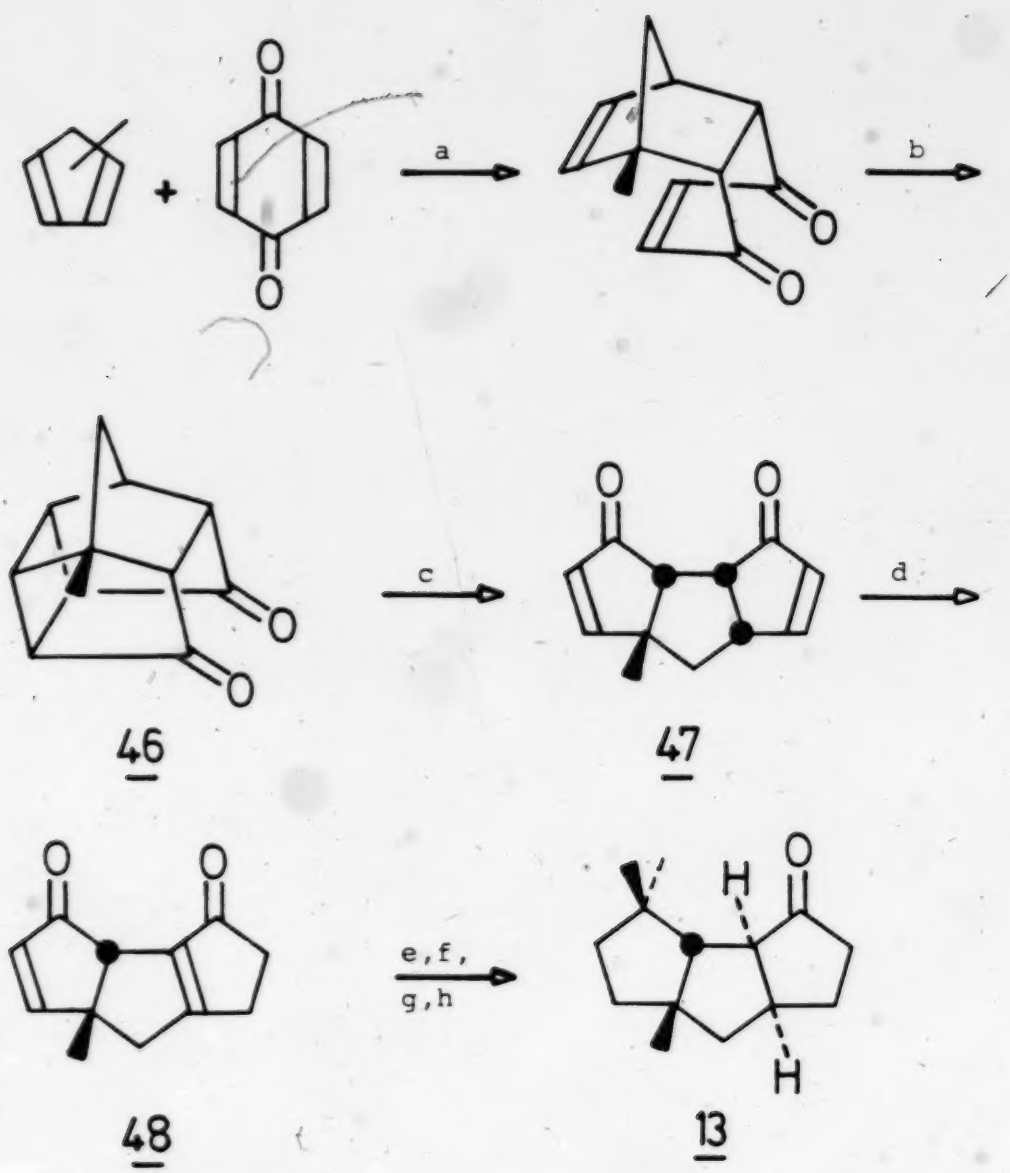
a.CH_2=CHLi. b.$SOCl_2$,room temperature. c.Mg,powder. d.60°C. e.CH_2=CHCHO. f.O_2. g.PDC,DMF. h.MeLi. i.O_3;Me_2S. j.KOH. k.Pt,H_2.l.CH_2=PPh_3.

produced the bicyclo[3.3.0]octane derivative **45**. This compound was converted to the keto-aldehyde **17** which in turn was transformed into $\Delta^{9(12)}$-capnellene (**2**) following Paquette's procedure.[12]

The tricyclic ketone **13** was efficiently prepared from the cage diketone **46** by Mehta and co-workers[18] (Scheme VIII). Diels-Alder reaction of methylcyclopentadiene and benzoquinone followed by irradiation of the adduct readily produced the diketone **46**. Vacuum pyrolysis of this diketone gave the cis-syn-cis triquinane system **47** which was isomerized to the compound **48** under basic conditions. Through a series of reactions this bis enone was eventually converted to the known ketone **13**.

The latest synthesis of $\Delta^{9(12)}$-capnellene (**2**) was reported by Piers and co-workers.[19] In their synthesis, 2-methyl-2-cyclopentenone was used as the ring B precursor of the target molecule (Scheme IX). To construct ring A, a copper mediated conjugate addition of 4-chloro-2-lithio-1-butene to the starting enone was carried out. Cyclization of the resulting chloroketone **49** induced by potassium hydride gave the required bicyclo[3.3.0]octanone derivative **50**. After reduction of this ketone to the corresponding alcohol, the gem-dimethyl group was fabricated from its exo-methylene functionality to get the compound **51** which was further converted to the enone **52**. Repeti-

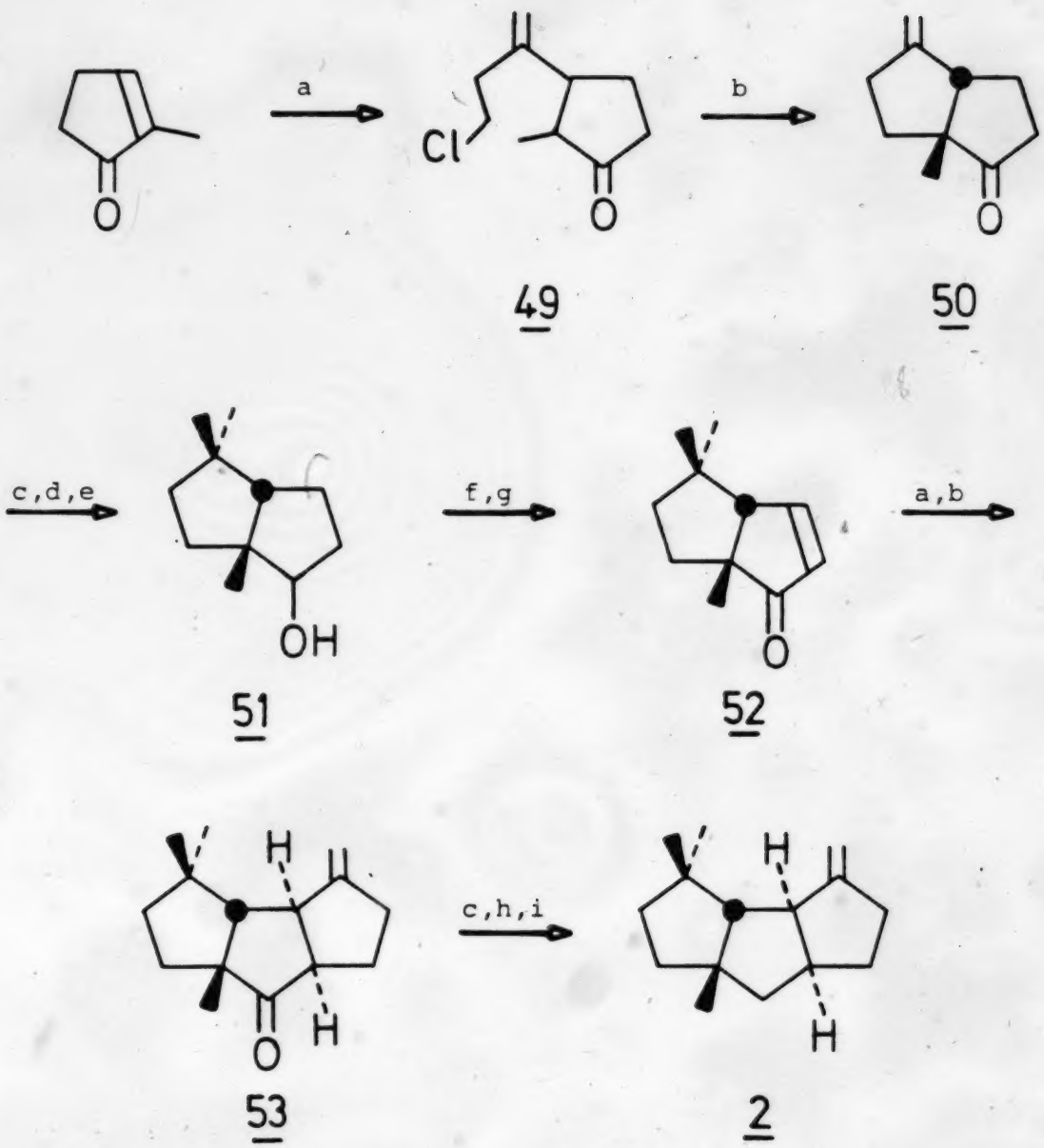
Scheme VIII



46 47 48 13

a.THF,room temperature. b.hν,EtOAc. c.vacuum pyrolysis.
d.DBU,CH_2Cl_2,reflux. e.H_2,Pd/C,EtOAc. f.$CH_2=PPh_3$.
g.CH_2I_2,Zn/Cu couple. h.H_2,Pt,AcOH.

Scheme IX



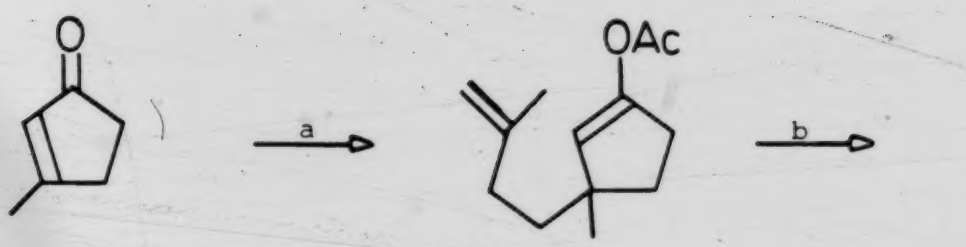
a.$ClCH_2CH_2C(CH_2)SnMe_3$,MeLi,$MgBr_2$,CuBr.Me_2S. b.KH. c.LAH. d.CH_2I_2,$ZnEt_2$,O_2,60°C. e.H_2,Pt,AcOH. f.PCC,CH_2Cl_2. g.TMSI, $Pd(AcO)_2$,MeCN, h.NaH,CS_2;MeI. i.n-Bu_3SnH,AIBN,PhMe,reflux.

tion of the conjugated addition-cyclization sequence on the enone **52** led to the required cis-anti-cis triquinane system **53**. Finally, reduction of the ketone **53** to the corresponding alcohol followed by deoxygenation via the corresponding xanthate furnished $\Delta^{9(12)}$-capnellene (**2**).

Recently, Pattenden et al.[20] achieved the synthesis of $\Delta^{9(12)}$-capnellene-8α,10α-diol, the C-8 (capnellane numbering) epimer of the naturally occurring diol **3** (Scheme X). Conjugate addition of lithium bis(3-methyl-but-3-enyl)cuprate to 3-methyl-2-cyclopentenone followed by trapping the resultant enolate with acetic anhydride furnished the enol acetate **54**. Treatment of this enol acetate with stannic chloride gave the bicyclo[3.3.0]-octane derivative **55** which was further converted to the keto-acetylene **56**. Reductive cyclization of this keto-acetylene with sodium naphthalene radical anion gave $\Delta^{9(12)}$-8-deoxycapnellene-10α-ol **57** in low yield. Finally, allylic oxidation of **57** furnished $\Delta^{9(12)}$-capnellene-8α,10α-diol **58**, an unnatural capnellanoid.

Very recently, a highly stero- and regioselective synthesis of $\Delta^{9(12)}$-capnellene (**2**) has been achieved in our laboratory by a flexible strategy that, in contrast to virtually all of those employed in the existing syntheses, can also be adapted to the synthesis of oxygenated capnellanoids found in the nature. Thus starting from 2-

Scheme X



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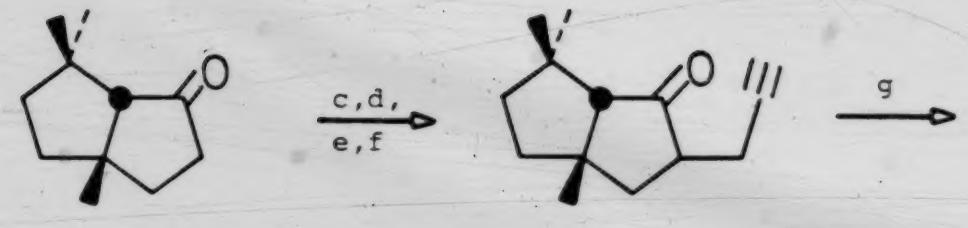
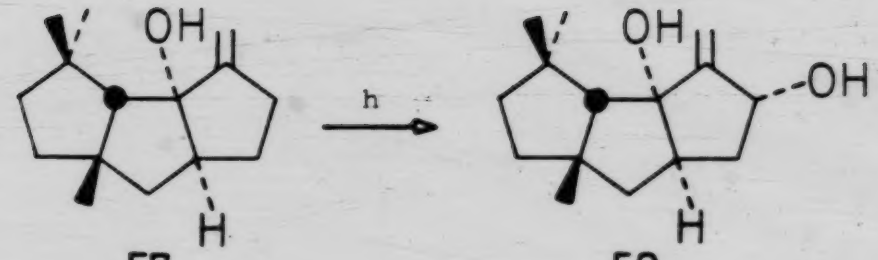


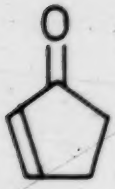
55 56



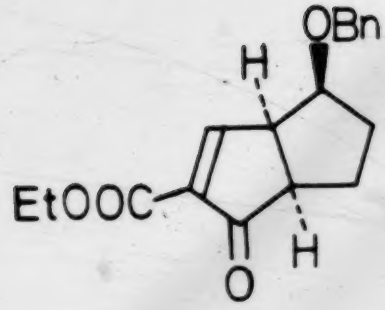
57 58

a. $[CH_3C(CH_2)CH_2CH_2]_2CuLi$; Ac_2O. b. $SnCl_4$. c. $KN(SiMe_3)_2$, $ICH_2CHClCH_2$. d. LAH. e. $KNHCH_2CH_2CH_2NH_2$. f. PCC, CH_2Cl_2. g. THF, Na-naphthalene radical anion. h. Me_3COOH, SeO_2.

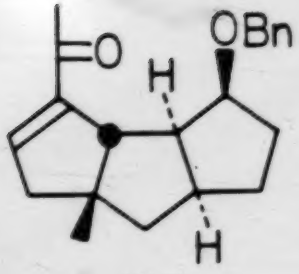
cyclopentenone (**59**), the ring C equivalent, two key intermediates **70** and **107** were prepared. In the preparation of the keto-ester **70** the key role was played by the combination of a photocycloaddition and a ring expansion reaction while the enone **107** was prepared by using Diels-Alder reaction and a ring contraction process as the key operations. This thesis describes the details of the synthetic work.



59



70



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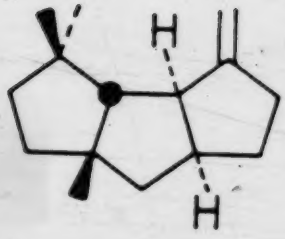


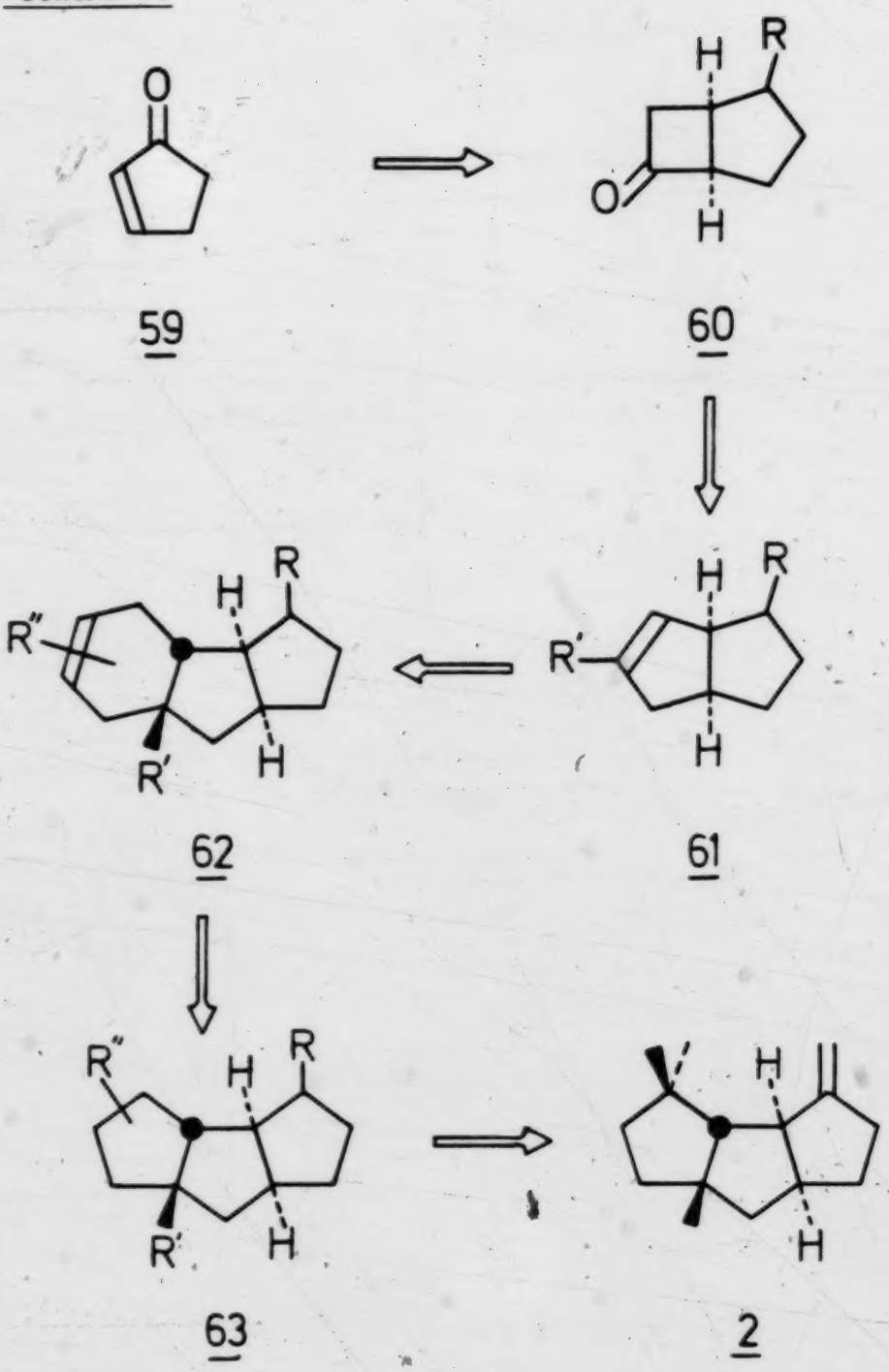
2

DISCUSSION

On the basis of the retrosynthetic analysis (Scheme XI), 2-cyclopentenone (**59**) could be envisaged as a ring C equivalent and a starting point for the synthesis of $\Delta^{9(12)}$-capnellene (**2**). Through a photochemical process, this enone could conceivably be converted to a bicyclo-[3.2.0]heptanone derivative **60**. A one carbon ring expansion of **60** could lead to an olefin **61**, thereby establishing the B/C ring unit of the capnellane skeleton. Subsequent Diels-Alder reaction of **61** with a suitable diene would result in the formation of the tricyclic compound **62**. A ring contraction process (**62** → **63**) followed by the adjustment of the existing functionalities could furnish the natural product **2**.

Based on the above analysis, our immediate synthetic goal was the preparation of a bicyclo[3.2.0]heptanone derivative of type **60**. This could, in principle, be accomplished by a photochemical addition of a ketene equivalent, in a head-to-tail fashion, to the carbon-carbon double bond of the starting enone **59**. Of the several readily available ketene equivalents, allene[21] is known to give the head-to-head regioisomer while vinyl esters[22a,b] and 1,1-dialkoxyethenes[23,24,25] are known to effect the head-to-tail addition. Of the latter two types

Scheme XI



59 60 62 61 63 2

of compounds 1,1-dialkoxyethenes are known to exert a better regiochemical control.[23] Thus, 1,1-diethoxyethene was selected as the ketene equivalent. This compound was readily prepared in large quantity by dehydrobromination of bromoacetaldehyde diethylacetal* according to the literature procedure.[26]

Irradiation of a benzene solution[23] of 2-cyclopentenone** (**59**) and a ten-fold excess of 1,1-diethoxyethene with a Hanovia 450 W medium pressure mercury vapour lamp using a pyrex filter afforded the 1:1 photoadduct as a single product in 85% yield. An absorption band at 1740 cm^{-1} in the IR spectrum was attributed to the five-membered saturated ketone. The mass spectrum showed a molecular ion peak at 198.1254 corroborating well with the molecular formula $C_{11}H_{18}O_3$. Four quartets at δ 3.39, 3.40, 3.45 and 3.46 (J = 7 Hz each) and two triplets at δ 1.18 and δ 1.21 (J = 7 Hz each) in the proton NMR spectrum were characteristic for the ethoxy groups. The regiochemical assignment of the photoadduct **64**** follows from the

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* Bromoacetaldehyde diethylacetal is commercially available. It can also be prepared easily from vinyl acetate.[27]

** 2-Cyclopentenone is commercially available. It can also be prepared on large scale from cyclopentadiene according to the literature procedure.[28]

*** With regard to its stereochemical assignment, the alternative trans arrangement is not feasible in bicyclo[3.2.0]heptane system.

previous observation[23] that the photocycloaddition of 2-cyclopentenone (**59**) with 1,1-dimethoxyethene gave only the head-to-tail regioisomer.

The ketone carbonyl of the compound **64** was conceived as a latent exo-methylene group required for $\Delta^{9(12)}$-capnellene (**2**). Conversion of the carbonyl group of **64** to a benzyl ether group via the corresponding alcohol was deemed appropriate for the preservation of this functionality. It was recognized that in so doing a new chiral center would be created. Although this center would be destroyed eventually and thus was of no consequence to the synthesis, in practice, it was highly desirable that a single stereoisomer be obtained. Lithium tri-t-butoxyalumino hydride[29] is known to reduce ketones in a highly stereoselective manner.[30] Accordingly, the ketone **64** was subjected to the reduction using this reagent. The alcohol thus obtained in quantitative yield was shown to be a single stereoisomer to which the structure **65** was assigned. The absorption band at 3440 cm^{-1} in the IR spectrum ensured the presence of the hydroxy group. This was further confirmed by the presence of a multiplet for the hydroxy substituted methine proton at δ 4.25 in the proton NMR spectrum. The molecular formula $C_{11}H_{20}O_3$ was correctly represented by the molecular ion peak at 200.1366 in the mass spectrum. Stereochemistry of the

newly created chiral center was assigned under the consideration that the reduction of the ketone should occur from the less hindered convex face of the molecule.

Subsequently, the benzyl ether **66** was obtained in 92% yield by treating the alcohol **65** successively with sodium hydride and benzyl bromide. The structure of this benzyl ether **66** was readily discerned from its spectral data. The proton NMR spectrum showed three singlets, one at δ 7.30 for the aromatic protons and the other two at δ 4.20 and 4.21 for the benzylic protons. The benzyloxy substituted methine proton appeared as a multiplet at δ 3.94 while two quartets at δ 3.38 and 3.39 (J = 7 Hz each) and two triplets at δ 1.17 and 1.19 (J = 7 Hz each) corresponded to the ethoxy groups. Although the mass spectrum failed to give a molecular ion peak, the presence of a fragment at m/e 245.1539 corresponding to the loss of an ethoxy unit supported the structural assignment.

Attempted hydrolysis of the ketal moiety of **66** with aqueous hydrochloric acid yielded only a small amount of the desired product **67**, presumably due to the decomposition of the product under the reaction conditions. This problem was circumvented by conducting the hydrolysis under mild reaction conditions. Treatment of the benzyl ether **66** with aqueous oxalic acid[31] produced the required cyclobutanone derivative **67** in near quantitative yield.

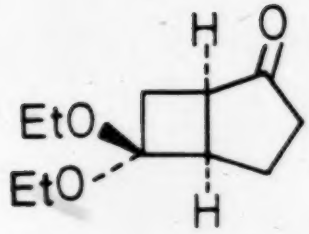
Absence of signals corresponding to the ethoxy groups in the NMR spectrum indicated the completion of the reaction. In the IR spectrum, the presence of an absorption band at 1770 cm^{-1} verified the formation of the four-membered ketone. The structure was further confirmed by the mass spectrum which displayed a molecular ion peak at 216.1158 equivalent to the molecular formula $C_{14}H_{16}O_2$.

It is noteworthy that, in the large scale (~50 g) preparation, the cyclobutanone **67** could be obtained in more than 75% yield from 2-cyclopentenone (**59**), in four steps without purification of the intermediates.

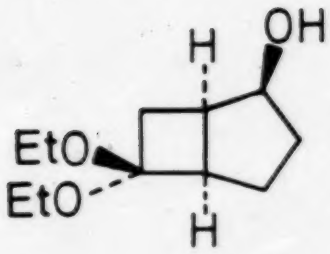
At this stage the expansion of the cyclobutanone ring of **67** by one carbon could establish the B/C ring unit of the capnellane skeleton. Of the several methods[32-36] available for this purpose, the direct ring expansion of cyclic ketones with boron trifluoride etherate and ethyl diazoacetate[35,36a,b,c] was most appealing. The reaction is known to proceed by the migration of the less substituted α-carbon atom chiefly.[36a,b,c] Application of this method to the cyclobutanone **67** would produce the keto-ester **68**, which would facilitate the preparation of the olefin of type **61** (Scheme XI) needed for the construction of ring A.

Treatment of an ethereal solution of the cyclobutanone **67** with boron trifluoride etherate and ethyl diazoacetate at 0°C produced a product which was found to be homogeneous by thin-layer chromatography (tlc). This product showed a molecular ion peak at 302.1511 in the mass spectrum and four intense absorption bands at 1750, 1723, 1660 and 1620 cm^{-1} in the IR spectrum. These spectral data were in agreement with the expected product **68**, existing partially in the enol form **68a**. The proton NMR spectrum was, however, complex and could not be explained on the basis of the presence of **68** and **68a** alone. Furthermore, the carbon-13 NMR spectrum displayed a total of sixty-six signals including three ketone carbonyl (δ 211, 213 and 214) and four ester carbonyl (δ 169.05, 169.52, 169.72 and 175.35) signals. On the basis of these spectral data and the fact that often a regioisomeric mixture is produced in the ring expansion reaction,[36b,c] it is very likely that the expected keto-ester **68** was formed along with the undesired regioisomer **69**; each of these regioisomers could exist as a mixture of epimers as well as in the corresponding enol forms i.e. **68a** and **69a**.*

* Subsequent transformation of this mixture furnished the enone **70** in 60% yield (vide infra). This suggested that the keto-ester **68** was the major constituent of the mixture at least to the extent of 60%.



64



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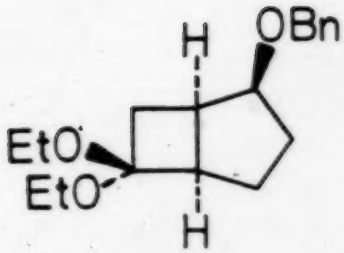
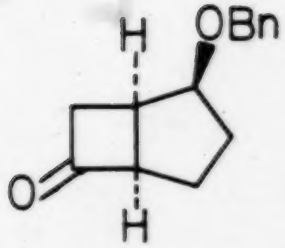
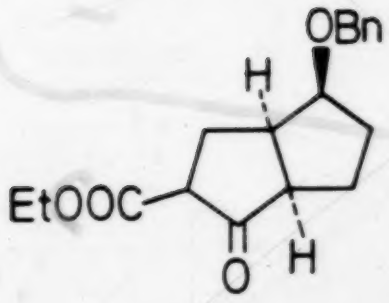


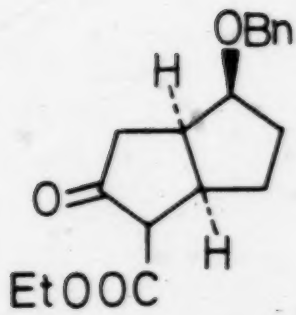
66



67



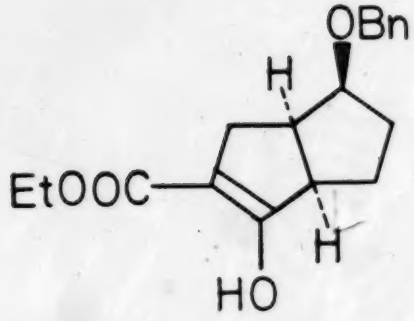
68



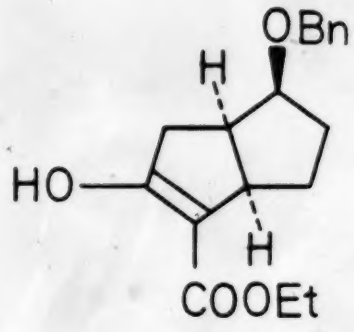
69

The conversion of the keto-ester **68** to the enone-ester **70**, required for the introduction of ring A via a Diels-Alder approach, was initially attempted by the use of direct methods. Thus, the keto-ester **68** was treated with selenium dioxide[37,38,39] in refluxing dioxane or with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[40a,b] in refluxing benzene. In each case the desired enone-ester **70** was produced, however, in a very poor yield (<20%). The yield of the enone-ester **70** was significantly improved when the recently developed indirect method based on the organoselenium chemistry[41,42,43] was applied. Thus, when the keto-ester **68** was treated with sodium hydride and phenylselenenyl chloride in tetrahydrofuran at room temperature, the corresponding selenide **71** was formed as a dark red liquid. A dichloromethane solution of the crude selenide **71** was treated with aqueous hydrogen peroxide to give, after purification by column chromatography, a 60% yield of the enone-ester **70**,* as a result of the oxidation and subsequent elimination of the selenyl group. The IR spectrum of **70** displayed two carbonyl absorptions at 1747 and 1720 cm^{-1}. The mass spectrum displayed a molecular

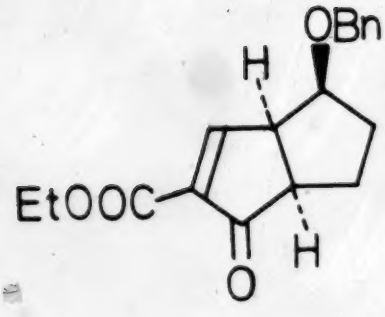
* This supports the inference reached (vide supra) that the keto-ester **68** is present to the extent of at least 60% in the product mixture obtained in the ring expansion reaction.



68a



69a



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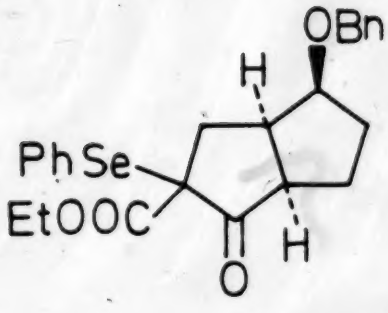
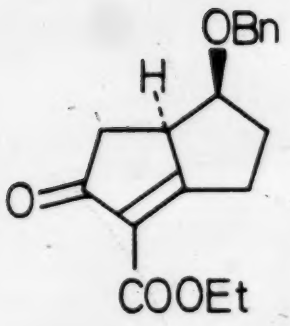


71

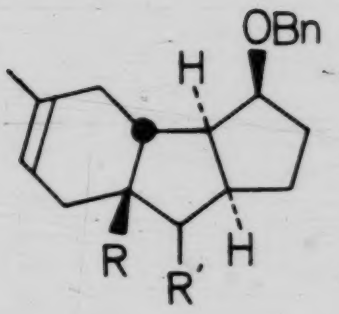


72

ion peak at 300.1366 equivalent to the molecular formula $C_{18}H_{20}O_4$. In the proton NMR spectrum, the benzyloxy substituted methine proton displayed a multiplet at δ 4.10 while a quartet at δ 4.30 (J = 7 Hz) and a triplet at δ 1.35 (J = 7 Hz) corresponded to the protons of the carboethoxy group. More importantly, the olefinic proton appeared as a doublet at δ 8.40 (J = 4 Hz). This unusually low field shift of the olefinic resonance was the result of the conjugation of the carbon-carbon double bond with two electron-withdrawing groups. The appearance of this olefinic proton in the NMR spectrum is in agreement with the structure of the enone-ester **70** and not with the isomeric compound **72**, which was not detected even though, its precursor, the keto-ester **69** was most likely present in the reaction mixture.

With the successful preparation of the enone **70**, a stage was set for the construction of the ring A of the capnellane skeleton via a sequence involving a Diels-Alder reaction and a ring contraction process. The latter process was intended to be carried out by oxidative cleavage of the cyclohexene ring produced in the Diels-Alder reaction followed by an intramolecular aldol condensation. In order to achieve a high degree of regiochemical control in the aldol condensation, isoprene was selected as the diene component in the Diels-Alder reaction. As indicated in Scheme XII, the oxidative

Scheme XII



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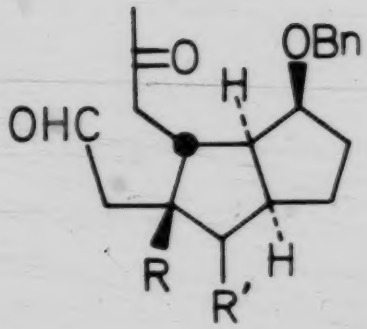

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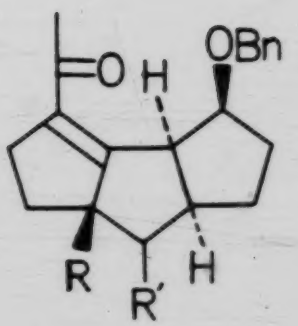


75

cleavage of the cyclohexene ring of the tricyclic compound **73** derived from isoprene and enone-ester **70**, should give the keto-aldehyde **74**. The aldol condensation of this keto-aldehyde should proceed in a completely regio-selective manner to give the enone **75**. Furthermore, the acetyl group in the enone **75** could be utilized as a handle for the incorporation of the gem-dimethyl moiety of $\Delta^{9(12)}$-capnellene (**2**).

It has been demonstrated that the Lewis acid catalyzed Diels-Alder reaction,[44,45] in comparison to the thermal one, normally proceeds at a faster rate and gives a better regio- and stereochemical control.[46a,b,c] Thus, the intended Diels-Alder reaction was explored under the Lewis acid catalysis. A solution of the enone-ester **70** in ether was treated with a large excess of isoprene in the presence of a catalytic amount (0.01 equiv.) of a Lewis acid such as ferric chloride, boron trifluoride etherate or stannic chloride at temperatures ranging from -78 to -30°C. In all the cases, the reaction failed to produce any detectable amount of product even after a reasonable period of time. As a result a larger amount of Lewis acid was used. Addition of one equivalent of ferric chloride to the reaction mixture at -78°C resulted in the rapid (less than three minutes) disappearance of the enone **70**. However, the product thus formed was found to be a complex

mixture of no less than four compounds. On the other hand, employment of one equivalent of boron trifluoride etherate at -78°C produced a single product. This product, however, failed to show the expected signal at around δ 1.60 for the vinylic methyl group in the NMR spectrum. Furthermore, the signal at δ 4.53, a typical value for the benzylic protons of the benzyl ether group, integrated for one proton only. Though the structure of this product could not be ascertained, the spectral data were incompatible with the structure of the desired Diels-Alder adduct. However, use of one equivalent of stannic chloride in the Diels-Alder reaction, to our delight, produced the adduct **76** (mp. 68-69°C) as a single product in 60% yield. The absorption bands at 1748 and 1725 cm^{-1} in the IR spectrum corresponded to the ester and the ketone carbonyls. The mass spectrum failed to show the expected molecular ion but registered a fragment at m/e 300.1366 corresponding to the loss of an isoprene unit as a result of a retro-Diels-Alder process. The elemental analysis corroborated well with the molecular formula $C_{23}H_{28}O_4$. The proton NMR spectrum displayed three singlets, a broad one at δ 5.44 for the olefinic proton and the remaining two at δ 7.30 and 1.68 for the aromatic and the vinylic methyl group. An AB quartet at δ 4.64 and 4.54 (J = 12 Hz each) was characteristic for the benzylic

protons while the benzyloxy substituted methine proton resonated at δ 4.04 as a multiplet. The protons of the carboethoxy group appeared as a quartet at δ 4.20 (J = 7 Hz) and a triplet at δ 1.34 (J = 7 Hz). The regiochemical assignment to the product followed from the well established pararule[47a,b,48] for the 2-substituted dienes. The stereochemistry was assigned in accordance with the "cis" principle[48] governing the Diels-Alder reaction and under the consideration that the diene should approach from the less hindered convex face of the dienophile **70**. The regio- and stereo-chemical assignment was shown to be correct by the eventual conversion of the adduct **76** to the natural product **2**.

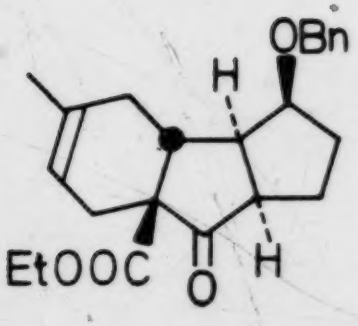
The ketone carbonyl of the Diels-Alder adduct **76** could give rise to the C-5 (capnellane numbering) hydroxy group of the naturally occurring capnellanoids **5** and **8**. However, for the synthesis of $\Delta^{9(12)}$-capnellene (**2**), the reduction of the ketone carbonyl to the corresponding methylene is essential. Also necessary is the reduction of the ester group of the adduct **76** to the hydrocarbon level to install the angular methyl group of the target molecule. Conventional methods for the direct reduction of ketones to hydrocarbons, such as Wolff-Kishner reduction and Clemmensen reduction employ strongly basic or acidic conditions. The compound **76** which possesses a

labile β-keto-ester functionality as well as a carbon-carbon double bond would not survive under these conditions. Another commonly used method to effect the reduction involves the formation of a thioketal followed by desulfurization with Raney nickel.[49] Towards this end, the adduct **76** was treated with boron trifluoride etherate in 1,2-ethanedithiol[50] at room temperature. Under these conditions, along with the expected thioketalization, the addition of 1,2-ethanedithiol to the carbon-carbon double bond and the debenzylation of the benzyl ether were observed. These side reactions could be suppressed by conducting the reaction in dichloromethane using two equivalents of 1,2-ethanedithiol and the desired thioketal **77** was obtained in a moderate yield of 45%. Several attempts to improve the yield, however, were not successful. That the thioketal was indeed formed was indicated by the presence of a complex multiplet between δ 3.32-3.06 corresponding to two methylene groups of the thioketal. Two singlets at δ 7.36 and 1.64 corresponded to the aromatic protons and vinylic methyl group, respectively. The benzylic protons appeared as an AB quartet at δ 4.65 and 4.52 (J = 12 Hz) while a broad doublet at δ 5.33 (J = 4 Hz) corresponded to the olefinic proton. The presence of a carbonyl absorption at 1722 cm^{-1} in the IR spectrum indicated that the ester group also has survived the

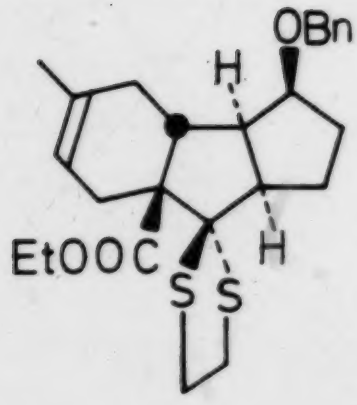
thioketalization conditions. The mass spectrum displayed a molecular ion peak at 444.1794 corresponding to the molecular formula $C_{25}H_{33}O_3S_2$ required for the thioketal **77**. The thioketal **77** was subjected to the treatment with Raney nickel in ethanol at room temperature. Unfortunately, the attempted desulfurization reaction showed lack of selectivity. In addition to the reduction of the thioketal, the carbon-carbon double bond was saturated and the benzyl ether was also cleaved. These results compelled us to explore other routes to remove the ketone group of the adduct **76**.

In principle, the reduction of the ketone carbonyl of the adduct **76** to the hydrocarbon level could be achieved indirectly by deoxygenation of the corresponding alcohol. In a similar manner, the ester group of the compound **76** could also be converted to the angular methyl group of the target molecule. Thus, it is conceivable that both of these transformations could be carried out simultaneously via the intermediacy of a 1,3-diol. Accordingly, the reduction of the keto-ester **76** was attempted with lithium aluminium hydride in tetrahydrofuran at room temperature. This reducing agent proved to be quite inefficient as a complex mixture of products was produced. To circumvent this problem, the keto-ester was subjected to reduction with other reducing agents. Sodium bis[2-

methoxyethoxy]aluminium hydride (SMEAH) is known to be as effective as lithium aluminium hydride in the reduction of ketones and esters.[51a,b] Moreover, being soluble in a wide range of organic solvents, this reagent, in comparison with lithium aluminium hydride, reduces the ketones and esters at a faster rate.[51c] Reduction of the keto-ester **76** with SMEAH in tetrahydrofuran at room temperature furnished, to our delight, the diol **78** (mp 136-137°C) as a single product in quantitative yield. The absence of the carbonyl absorption bands and the appearance of a new absorption band at 3360 cm^{-1} characteristic for the hydroxyl group, in the IR spectrum, showed the complete reduction of the ketone and the ester groups. In the NMR spectrum a doublet at δ 3.72 (J = 7 Hz) for a hydroxy substituted methine proton and an AB quartet at δ 3.70 and 3.50 (J = 12 Hz each) for the hydroxy bearing methylene group further supported the assigned structure **78**. The mass spectrum of this compound displayed a molecular ion at 328.2041 equivalent to the molecular formula $C_{21}H_{28}O_3$. Fragments at m/e 310.1930 and 292.1824, respectively corresponding to the loss of one and two water molecules, were also observed. SMEAH has been shown to be a weakly co-ordinating reducing agent.[52,53] Its initial co-ordination with the ester carbonyl and the ether oxygen of the adduct **76** should facilitate the



76



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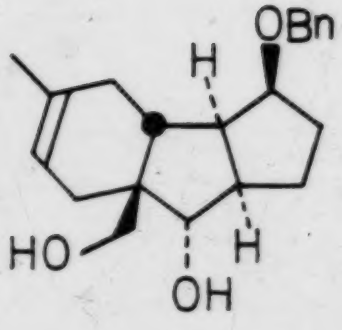

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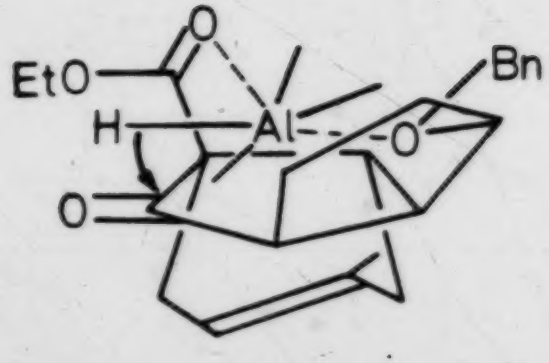


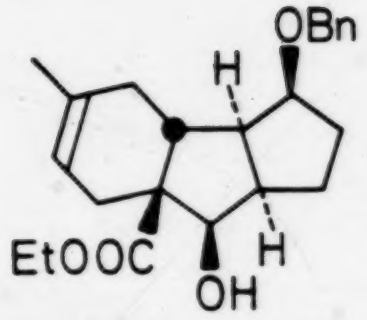
79

delivery of the hydride from the si face[54] of the ketone carbonyl as depicted in structure **79**. On the basis of this consideration, the "trans" stereochemistry was tentatively assigned to the diol **78**.

Reduction of the adduct **76** with potassium tri-s-butylborohydride (K-Selectride)[55a] in tetrahydrofuran at room temperature gave the mono-alcohol **80** which on further reduction with SMEAH furnished the diol **81** (mp 110-111°C) in 80% yield. This compound showed an absorption band for the hydroxy group at 3360 cm^{-1} in the IR spectrum and a molecular ion at 328.2041 equivalent to the molecular formula $C_{21}H_{28}O_3$ in the mass spectrum. However, the melting point and the chromatographic behaviour (tlc) of this compound were found to be different from those of the diol **78**. The proton NMR spectrum of the diol **81** displayed a double at δ 3.65 (J = 6 Hz) for the hydroxy substituted methine proton and an AB quartet at δ 3.66 and 3.57 (J = 12 Hz each) for the hydroxy bearing methylene group. Comparison of these values with those of the respective protons in the diol **78** further confirmed their non-identity. K-Selectride is known to be a non-coordinating[55a,b] reducing agent and it most probably reduces the ketone carbonyl of the adduct **76** from the less hindered si face.[54] On the basis of this assumption the "cis" stereochemistry was assigned to the diol **81**. The

stereochemical assignments made to the diols **78** and **81** were shown to be correct by subsequent transformations.

The conversion of the diol **78** or **81** to $\Delta^{9(12)}$-capnellene (**2**) would require two major operations: the removal of both the hydroxy groups (e.g., to **82**) and the modification of the cyclohexene ring. The synthesis could, in principle, proceed with either of these operations. It was felt that it would be advantageous to modify the cyclohexene ring prior to the removal of the hydroxy groups. To explore the feasibility of the ring contraction process, the diol **78** was converted to the diacetate **83** with acetic anhydride in pyridine. Treatment of this diacetate with osmium tetroxide-sodium meta-periodate[56] in dioxane at room temperature resulted in the formation of a complex mixture of products. However, when the diacetate **83** was ozonolyzed in dichloromethane at -78°C and the resulting ozonide was reduced with dimethyl sulfide, to our delight, the desired enone **84** was formed in 60% yield. Apparently, the intermediate keto-aldehyde **85**, produced by the ozonolysis-reduction process, underwent further aldol condensation to give directly the enone **84**. The IR spectrum recorded two intense absorption bands at 1740 and 1660 cm^{-1}, respectively, for the acetate and the conjugated enone carbonyls. The proton NMR spectrum displayed four singlets - a rather broad one at δ 6.60 for



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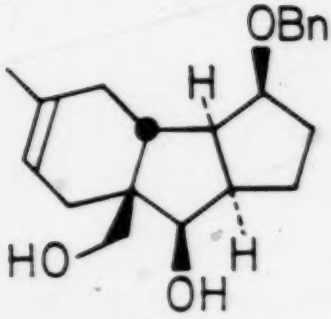
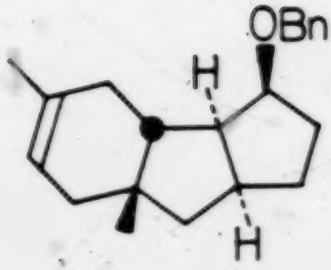


81



82

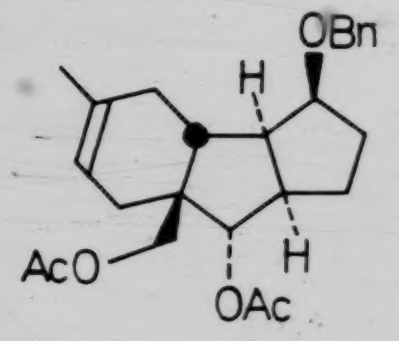
the β-proton of the conjugated enone and three sharp ones at δ 2.30, 2.06 and 1.84 for two acetate and one acetyl methyl groups. The mass spectrum of the enone **84** showed a molecular ion peak at 426.2035 corresponding to the molecular formula $C_{25}H_{30}O_6$.

The efficient conversion of the diacetate **83** to the enone **84** indicated that the ring A of $\Delta^{9(12)}$-capnellene (**2**) could be constructed via a process involving ozonolysis and intramolecular aldol condensation. However, the acetate was considered to be inadequate as a protecting group for the hydroxyls of the diol **78** and **81**, as it would probably not survive under the conditions required for further transformations. Furthermore, the use of acetate for the protection of hydroxy groups would require additional synthetic operations for the deprotection and subsequent activation of the hydroxy groups for their ultimate removal. Consequently, a more stable protecting group which also could serve as an activating group for the ultimate removal of both the hydroxyls was highly desirable.

Recently, Ireland[57] has reported the preparation of N,N,N',N'-tetramethylphosphorodiamidate derivatives of the alcohols using N,N,N',N'-tetramethyldiamidophosphorochloridate as a phosphorylating agent. Liu and coworkers[58] have later on developed a modified procedure for

the preparation of these derivatives from sterically hindered alcohols, which involves the treatment of an alcohol with a more reactive reagent, N,N-dimethylamidophosphorodichloridate, followed by quenching the reaction with anhydrous dimethylamine. The phosphorodiamidate derviatives are known to be rather stable compounds[57,58] which are unreactive under mild acidic, basic and hydrogenation conditions, as well as towards the metal hydride reducing agents. However, when subjected to the dissolving metal reductions, these compounds were shown to undergo carbon-oxygen bond cleavage to give the corresponding hydrocarbons.[57,58] These properties of the phosphorodiamidate derivatives could be utilized for the protection as well as the activation of the hydroxyls. Thus, to investigate the feasibility of this method the preparatión of the bisphosphordiamidates **86** and **89** from diols **78** and **81**, respectively, was attempted.

Treatment of the trans diol **78** with sodium hydride and N,N-dimethylamidophosphorodichloridate in tetrahydrofuran at room temperature followed by quenching the reaction with anhydrous dimethylamine gave a single product. The IR spectrum of this compound showed an intense hydroxyl absorption at 3360 cm^{-1} suggesting that the compound obtained was probably a monophosphorodiamidate derivative rather than the desired compound **86**.



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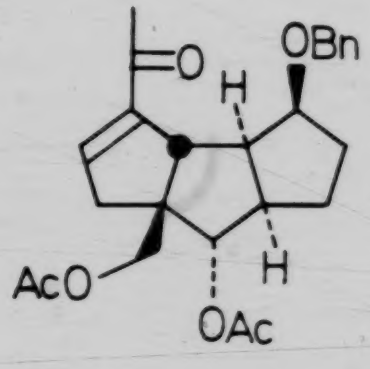

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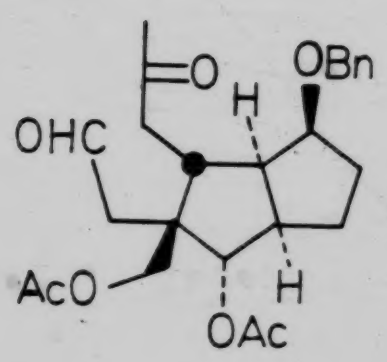

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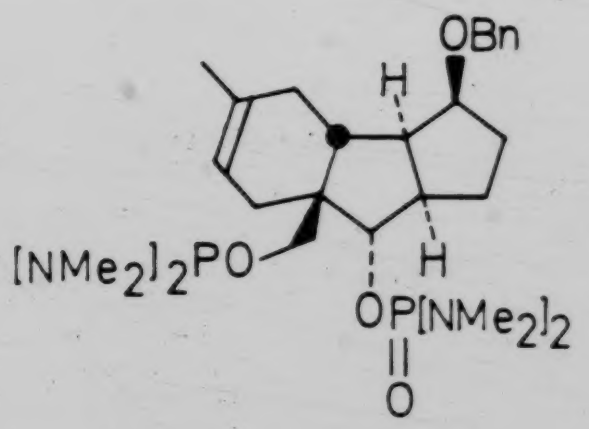

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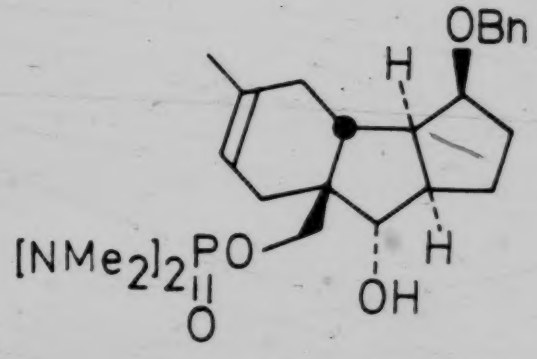

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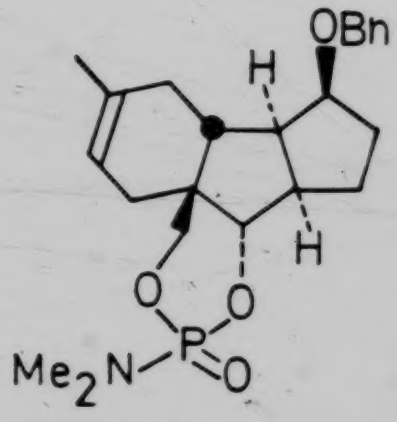


88

This was confirmed by the mass spectrum which displayed a molecular ion at 462.2651, equivalent to the molcular formula $C_{25}H_{39}O_4N_2P$. The proton NMR spectrum showed two doublets at δ 2.68 and 2.66 (J = 10 Hz each) corresponding to two dimethylamino groups. The downfield shift of the signals at δ 3.70 and 3.50, observed for the hydroxymethylene protons of the starting diol **78**, to δ 3.85 and 3.70 further suggested that the primary hydroxyl was selectively phosphorylated. Accordingly, the structure **87** was assigned to this compound. The failure of the diol **78** to undergo bisphosphorylation could be rationalized on steric grounds. Being adjacent to a quaternary center as well as being endo-oriented with respect to the bicyclo-[4.3.0]nonane system, the secondary hydroxyl is extremely congested. This contributes to its low reactivity towards a bulky reagent. It should be noted that the diol **78** could, in principle, react with N,N-dimethylamidophosphorodichloridate to give the cyclic phosphoramidate **88** which, however, was not formed presumably due to the trans-orientation of the hydroxy and the hydroxymethyl groups. The assigned stereochemistry agrees well with these observations.

Under similar conditions, treatment of the cis-diol **81** with sodium hydride and N,N-dimethylamidophosphoramide in tetrahydrofuran at room temperature followed by

quenching the reaction with anhydrous dimethylamine also gave a single product. The absence of hydroxyl absorption band in its IR spectrum indicated that both the hydroxyls were phosphorylated. In the NMR spectrum, the downfield shift of the signal for the hydroxymethine proton of diol **81** at δ 3.65 to δ 4.53 and a similar downfield shift of the signals for the hydroxymethylene protons at δ 3.66 and δ 3.56 to δ 4.32 and δ 4.05 further suggested that the phosphorylation of both the hydroxyls had occurred. The presence of one doublet at δ 2.69 (J = 10 Hz) integrating for six protons indicated that the compound possesses only one dimethylamino group. The cyclic phosphoramidate **90** rather than the bisphosphorodiamidate **89** corroborates well with the above spectral data. The mass spectrum confirmed the above structural assignment by displaying a molecular ion peak at 417.2063 corresponding to the molecular formula $C_{23}H_{32}O_4NP$. The facile formation of the cyclic phosphoramidate **90** from the diol **81** and the formation of only the monophosphorodiamidate **87** from the diol **78** lend substantial support to the stereochemistry assigned to these diols.

Although the cyclic phosphoramidate group in **90** would adequately serve the purpose of protecting the 1,3-diol through the ensuing transformations, the behaviour of such cyclic phosphoramidates in the dissolving metal reduction

reactions is not known. It was thus necessary to study the dissolving metal reduction of the cyclic phosphoramidate **90** before proceeding with the synthesis. Treatment of the phosphoramidate **90** with lithium-ethylamine[57] in tetrahydrofuran at 0°C furnished a single product. The IR spectrum displayed an intense hydroxyl absorption at 3360 cm^{-1}. In the proton NMR spectrum, the signals characteristic for the benzyl group were absent. These observations indicated that the reductive removal of the benzyl protecting group had regenerated the hydroxy group. The proton NMR spectrum also displayed a sharp methyl singlet at δ 1.06 suggesting that the primary carbon-oxygen bond of the cyclic phosphoramidate group was reductively cleaved. The presence of a molecular ion peak at 222.1623 corresponding to the molecular formula $C_{14}H_{22}O_2$ along with the fragments at m/e 204.1514 and 186.1406 due to the loss of one and two water molecules, respectively, in the mass sepctrum strongly suggested that the product in hand is the diol **91**. The doublet at δ 3.32 for a hydroxymethine proton adjacent to only one hydrogen atom and a multiplet at δ 4.0 for a second hydroxymethine proton in the proton NMR spectrum corroborated well with the diol structure **91**. This result showed that the dissolving metal reduction of a cyclic phosphoramidate, like **90**, derived from a 1,3-diol leads to the cleavage of

only one carbon-oxygen bond selectively. This interesting result, though not useful for the present purpose, may have potential applications in other areas of organic synthesis.

The efforts directed towards the preparation of the bisphosphorodiamidates **86** and **89** led to the following conclusions. In the first place, their preparation, respectively from diols **78** and **81** could not be realized. Secondly, though both the hydroxyls of **81** could be protected as the cyclic phosphoramidate **90**, their simultaneous removal via **90** was not possible. Thus, it was realized that the ability of a phosphoramidate group to serve both as a protecting group as well as an activating group could not be effectively exploited to the benefit of the synthesis. At this stage it was decided to convert the diol **78** or **81** to **82** prior to the modification of the cyclohexene ring.

Recently it has been reported[59a,b,c,d] that the photolysis of acetates at 254 nm in aqueous hexamethylphosphoramide effects carbon-oxygen bond cleavage to provide the corresponding hydrocarbons. Accordingly, the diacetate **83** was dissolved in hexamethylphosphoramide containing 10% water and irradiated at 254 nm in a Rayonet mini-reactor. However, the starting diacetate **83** was recovered unchanged from the reaction mixture.

It is well known that the sulfonates of simple alcohols can be reduced to the corresponding hydrocarbons with lithium aluminium hydride,[60,61,62,63] sodium cyanoborohydride,[64,65,66] and lithium triethylborohydride,[67,68,69,70] thus indirectly effecting the deoxygenation of alcohols. It has also been shown that even the sterically hindered mesylates can be reduced when the reduction is carried out in the presence of a transition metal salt such as nickel chloride,[71] cobalt chloride[72] and copper(I) chloride.[73] To apply these methods, the dimesylate **92** was prepared by treating the diol **78** with methanesulfonyl chloride[74] and triethylamine in dichloromethane at room temperature. The mesylate **92** was subsequently subjected to the treatment with several reducing agents such as lithium aluminium hydride, sodium cyanoborohydride and lithium triethylborohydride under various conditions. These attempted reductions invariably gave the diol **78** in quantitative yield as a result of the cleavage of the sulfur-oxygen bond. These findings are in agreement with the reported observations on hindered mesylates.[75] Even when the reduction was carried out in the presence of a transition metal salt such as nickel chloride[71] and cobalt chloride,[72] the diol **78** was produced in quantitative yield.

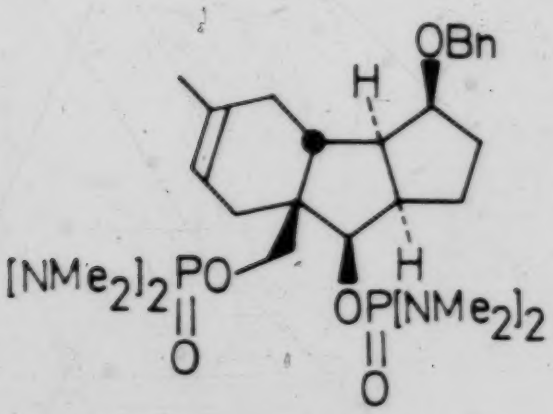
Recently, two additional methods have been developed

for the reduction of sulfonates. Shono et al.[76] has demonstrated that electrolysis of mesylates, including the hindered ones, produces the corresponding hydrocarbons. The other method developed by Fujimoto et al.[77] involves the heating of a mesylate with zinc dust and sodium iodide in a polar solvent such as dimethoxyethane, dimethylformamide, dimethylsulfoxide and hexamethylphosphoric triamide. Both of these methods were attempted. Electrolysis of the mesylate **92** under the reported conditions[76] however failed to effect its reduction and the starting material was recovered quantitatively. On the other hand, when the dimesylate **92** was heated with zinc and sodium iodide in dimethylformamide at 145°C, to our delight, a non-polar product was formed. The proton NMR spectrum of this compound showed no signals characteristic of the mesyl group indicating that both the mesylates have been removed. It further displayed a singlet at δ 7.34 for the aromatic protons, an AB quartet at δ 4.61 and 4.47 (J = 12 Hz each) for the benzylic protons, a multiplet at δ 3.79 for the benzyloxymethine proton, and two broad singlets at δ 5.46 and 1.70 respectively for the olefinic proton and the vinylic methyl group. These spectral data indicated that the benzyl ether and the carbon-carbon double bond have survived the reaction conditions. The absence of a signal corresponding to the angular methyl group,

however, suggested that the product was probably not the expected compound **82**. The appearance of a doublet of doublets (J = 4 Hz, J' = 8 Hz) at an abnormally high field of δ 0.16 in the proton NMR spectrum suggested that the compound is a cyclopropyl derivative. Accordingly, the structure **93*** was assigned. This assignment was confirmed by the presence of a molecular ion at 294.1975, equivalent to the molecular formula $C_{21}H_{26}O$, in the mass spectrum. The formation of compound **93** could be rationalized by invoking an organozinc intermediate such as **94** which could undergo cyclization[78] via a S_N2' type displacement leading to the observed product. It is conceivable that such a ring closure could be suppressed by the use of the cis analogue of the dimesylate **92** as a starting material.

The cis dimesylate **95** was easily prepared by treating the diol **81** with methanesulfonyl chloride and triethylamine in dichloromethane.[74] On heating the dimesylate **95** with zinc dust and sodium iodide in dimethylformamide at 145°C, a single compound was formed. This compound was shown to be different from the cyclopropane **93** by direct comparison. A careful study of its spectral data showed that the compound was the monoalcohol **96** and not the

* A decoupling experiment located the other two cyclopropyl protons at δ 1.24 and 1.30.



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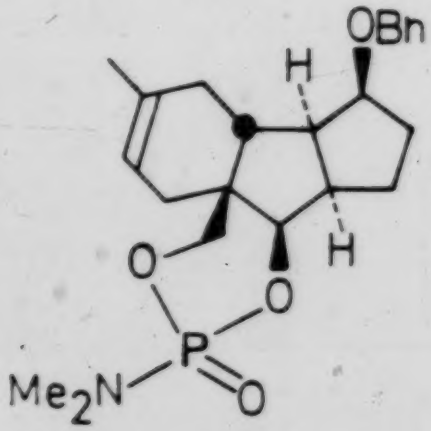

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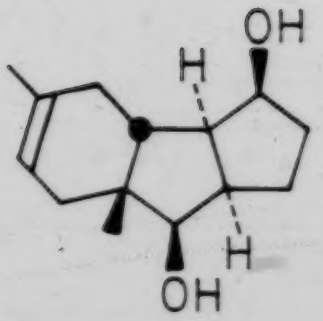

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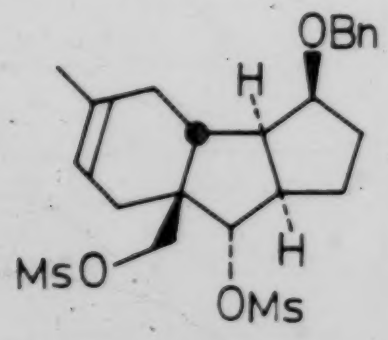

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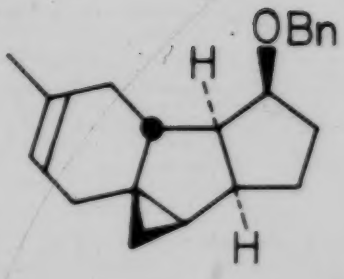

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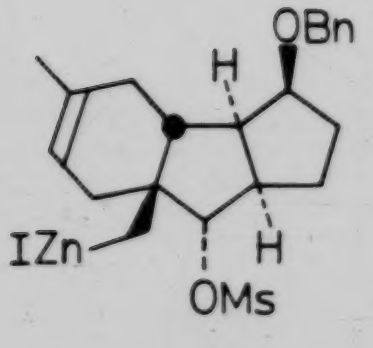


94

expected benzyl ether **82**. The IR spectrum showed a hydroxyl absorption band at 3360 cm^{-1}. In the proton NMR spectrum the angular methyl resonated at δ 1.02 and the hydroxymethine proton appeared at δ 3.46 as a doublet (J = 5 Hz). The mass spectrum displayed a molecular ion at 312.2084 corresponding to the molecular formula $C_{21}H_{28}O_2$. As the attempts to remove both the hydroxyls of the diol **78** or **81** via their mesylates did not succeed, other methods were explored to achieve this transformation.

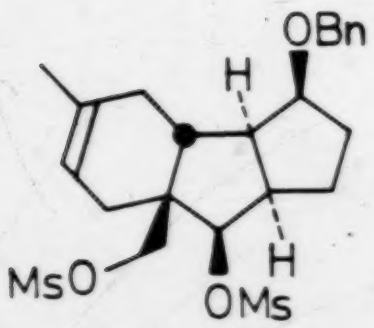
Barton[79] and others[84] have demonstrated that on reaction with tri-*n*-butylstannane, *S*-alkyl xanthates, derived from the corresponding alcohols, yield related hydrocarbons. It was further demonstrated that the related derivatives such as thionobenzoate,[79,82] thiocarbonyl immidazolide,[79,83] thioformates[80] and phenoxy thionocarbonate[81] also undergo the above transformation. The application of such a reaction to the diol **78** or **81** should, in principle, provide the desired compound **82**. Initial attempts to convert the diol **78** to the corresponding bisxanthate with carbon disulfide and methyl iodide failed to give any reaction product. Consequently, the reaction of the diol **78** with phenoxythiocarbonyl chloride[81] was examined. When the diol **78** was treated with phenoxythiocarbonyl chloride and 4-(*N*,*N*-dimethyl-

amino)pyridine in acetonitrile at room temperature, a single product was formed. Its spectral data showed that this compound was the monothionocarbonate **97** rather than the expected bisthionocarbonate derivative **98**. The hydroxymethine proton appeared as a doublet (J = 7 Hz) at δ 3.60 in the NMR spectrum while the AB quartet (J = 12 Hz each) of the hydroxymethylene protons of the starting diol **78** at δ 3.70 and 3.50 now appeared at δ 4.58 and 4.28 (J = 12 Hz each). Though the mass spectrum failed to display a molecular ion, a fragment at m/e 370.1602, resulting from the loss of a phenol molecule, was registered. The fact that the diol **78** failed to give the bisthionocarbonate **98** once again indicated that the simultaneous derivatization of both the hydroxyls with a rather bulky reagent was difficult. When the deaerated solution of the thionocarbonate **97** in toluene was treated with one and half equivalents of tri-n-butylstannane and a catalytic amount of 2,2'-azobis[2-methyl-2-propionitrile] and refluxed for 3 h, the monoalcohol **99** was formed in 60% yield (over two steps from **78**). The IR spectrum showed a hydroxyl absorption at 3440 cm^{-1}. The proton NMR spectrum showed a methyl singlet at δ 0.98 and a doublet (J = 7 Hz) for the hydroxymethine proton at δ 3.30. The mass spectrum displayed a molecular ion peak at 312.2081 equivalent to the molecular formula $C_{21}H_{28}O_2$ along with a fragment at

m/e 294.1978 resulting from the loss of a water molecule.

As a consequence of the unsuccessful attempt to simultaneously derivatize both the hydroxyls of the diol **78**, we turned our attention to the cis-diol **81**. Treatment of the diol **81** with an excess of phenoxythiocarbonyl chloride and 4-(N,N-dimethylamino)pyridine in acetonitrile gave the cyclic thionocarbonate **100** in a moderate yield. The IR spectrum of this compound showed no hydroxyl absorption. In the proton NMR spectrum, the methine proton of the cyclic thionocarbonate group gave a doublet at δ 4.00 (J = 6 Hz) while the methylene protons appeared as an AB quartet at δ 4.08 and 4.20 (J = 11 Hz each). The mass spectrum showed a molecular ion peak at 370.1605 equivalent to the molecular formula $C_{22}H_{26}O_3S$. Barton[85] has reported that the treatment of a six-membered cyclic thionocarbonate, derived from a primary and a secondary alcohol, with tri-n-butylstannane results in the cleavage of the secondary carbon-oxygen bond selectively. Surprisingly however, treatment of the cyclic thionocarbonate **100** with two equivalents of tri-n-butylstannane and a catalytic amount of 2,2'-azobis[2-methyl-2-propionitrile] in refluxing toluene for 3 h resulted in the complete recovery of the starting material.

The results of the experiments carried out for the simultaneous removal of the hydroxyls of the diols **78** and



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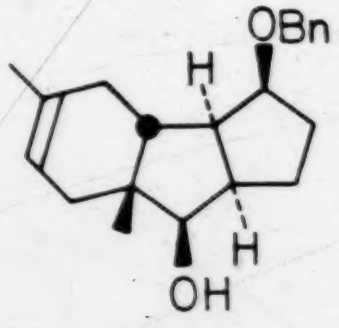

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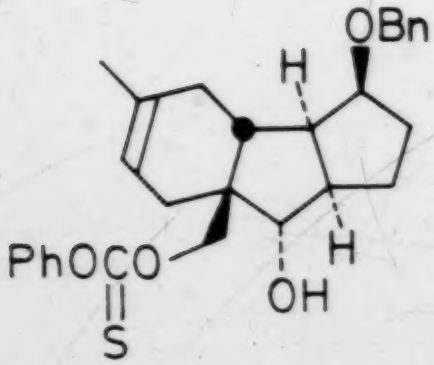

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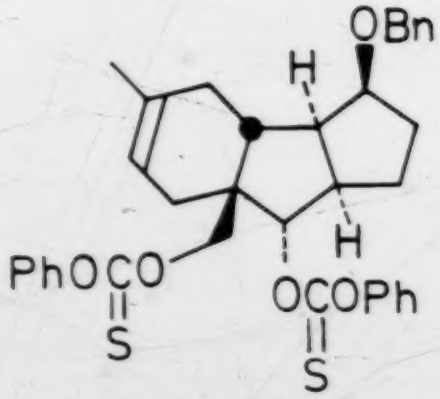

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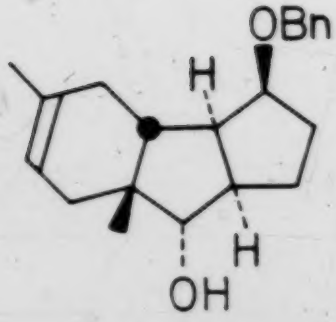

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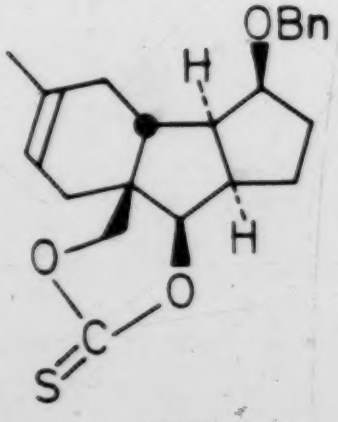


100

81 to produce the compound **82** clearly indicated that such conversion could not be achieved easily. In order to circumvent this problem it was decided to remove the hydroxyls in a stepwise manner. In this regard the monoalcohol **96**, obtained from diol **81** by zinc-sodium iodide reduction of the corresponding dimesylate **95**, and the monoalcohol **99** obtained from the diol **78** via tri-n-butylstannane reduction of the thionocarbonate **97**, were the obvious intermediates to proceed with the synthesis. To effect the deoxygenation of these monoalcohols **96** and **99** the phosphorodiamidate method was initially attempted.

The monoalcohol **96** was treated with sodium hydride and N,N-dimethylamidophosphorodichloridate in tetrahydrofuran at room temperature. Quenching of the reaction mixture with anhydrous dimethylamine gave the phosphorodiamidate **101** in 60% yield. The IR spectrum showed the absence of a hydroxyl absorption. In the proton NMR spectrum the doublet of doublets (J = 6 Hz, J' = 10 Hz) at δ 4.27 corresponded to the proton adjacent to the phosphoramidate group while the two dimethylamino groups gave two doublets (J = 10 Hz each) at δ 2.85 and 2.70. The mass spectrum registered a molecular ion at 446.2700 equivalent to the molecular formula $C_{25}H_{39}H_2O_3P$ along with a fragment at m/e 294.1979, resulting from the loss of a tetramethylphosphoramidic acid molecule.

Similar treatment of the monoalcohol **99** with sodium hydride and N,N-dimethylamidophosphorodichloridate in tetrahydrofuran at room temperature followed by the addition of an excess of anhydrous dimethylamine gave the phosphorodiamidate **102** in 55% yield. The IR spectrum showed no absorption characteristic of the hydroxy group. In the proton NMR spectrum, the hydrogen atom adjacent to the phosphoramidate group resonated at δ 3.98 as a doublet of doublets (J = J' = 7 Hz) while two doublets at δ 2.72 and 2.70 (J = 10 Hz each) corresponded to two dimethylamino groups. The mass spectrum displayed a molecular ion at 446.2702 equivalent to the molecular formula $C_{25}H_{39}H_2O_3P$ along with a fragment at m/e 294.1986 resulting from the loss of a tetramethylphosphoramidic acid molecule.

The reduction of the phosphorodiamidates **101** and **102** was next examined. Treatment of the phosphoramidate **101** in tetrahydrofuran with lithium and ethylamine at 0°C gave the monoalcohol **103** in a moderate yield of 50%. The IR spectrum of this alcohol showed a hydroxyl absorption at 3380 cm^{-1}. The proton NMR spectrum showed no signals corresponding to the benzyl group. The olefinic proton appeared as a broad singlet at δ 5.30 while the vinylic and the angular methyls gave singlets respectively at δ 1.66 and 0.98. The hydroxymethine proton appeared as a

multiplet at δ 4.20. The mass spectrum showed the molecular ion at 206.1662 equivalent to the molecular formula $C_{14}H_{22}O$. The alcohol **103** was also obtained in 55% yield by the lithium-ethylamine reduction of the phosphoramidate **102** under similar conditions.

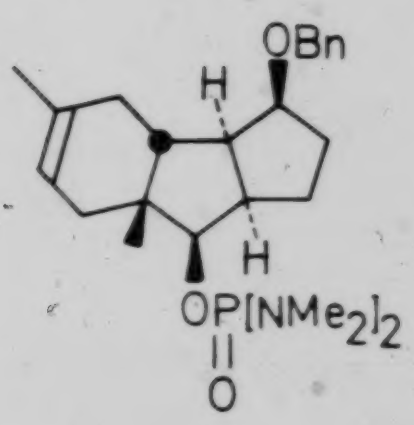
The above results showed that the phosphorodiamidate method could successfully be applied for the deoxygenation of the alcohols **96** and **99**. However, simultaneous cleavage of the benzyl group necessitates the reprotection of the resulting alcohol, prior to proceeding with the synthesis. This limits the synthetic utility of this method, in the present context, considerably. Consequently, other methods of deoxygenation were explored. It was also decided to focus our attention on the monoalcohol **99** since this alcohol can be prepared in three steps in an overall yield of 60% from the Diels-Alder adduct **76**, as compared to the 36% yield of the monoalcohol **96** obtained from the same compound over four steps. It is also noteworthy that the alcoholic group of the compound **99** and those of the capnellanoids **5** and **8** at C-5, possess the same configuration.

It was previously found that the reduction of the dimesylate **92** resulted in the formation of the cyclopropane derivative **93** (vide supra). In the absence of the primary mesylate, it was conceivable that the monomesylate

104 would undergo reduction giving rise to the desired compound **82**. The mesylate **104** was readily prepared by treating the alcohol **99** with methanesulfonyl chloride[74] and triethylamine in methylene chloride at room temperature. Subsequently, heating the mesylate **104** with zinc and sodium iodide in dimethylformamide at 145°C resulted in the formation of two compounds. The separation of these two compounds, although difficult, was achieved by chromatography on a silica gel column. A careful examination of the spectral data of the pure compounds revealed that the fast moving compound was the expected reduction product **82** and the slow moving compound was the diene **105**, formed by the elimination of the mesylate. In the proton NMR spectrum, the latter compound showed three singlets at δ 7.34, 1.70 and 1.10 respectively for the aromatic protons, the vinylic methyl group and the angular methyl group. The two olefinic protons gave rather broad singlets at δ 5.50 and 5.38. The benzylic protons appeared as an AB quartet (J = 12 Hz each) at δ 4.62 and 4.50 while the benzyloxymethine proton appeared as a multiplet at δ 3.80. The mass spectrum showed a molecular ion peak at 294.1984 equivalent to the molecular formula $C_{24}H_{26}O$. The compound **82** showed four singlets at δ 7.28, 5.28, 1.66 and 0.98 respectively for the aromatic protons, the olefinic proton and the vinylic and angular methyl

groups. The benzylic protons appeared as an AB quartet (J = 12 Hz each) at δ 4.60 and 4.51 while the benzyloxymethine proton gave a multiplet at δ 3.82. The mass spectrum registered a molecular ion peak at 296.2136 corresponding to the molecular formula $C_{21}H_{28}O$. A complete suppression of the side reaction leading to the formation of diene **105** could not be achieved either by changing the solvent (dimethyl sulfoxide, hexamethylphosphoramide, di-n-butyl ether) or the reagent (sodium, potassium and lithium iodide). The compound **82** was obtained in the best yield of 36% by heating the mesylate **104** with zinc and lithium iodide in dimethylformamide at 145°C. Under these conditions the diene **105** was also formed to the extent of 20%.

In an effort to improve the above conversion (**99** → **82**), several other deoxygenation methods were examined. Treatment of the alcohol **99** with phenyl chlorothionocarbonate and 4-(N,N-dimethylamino)pyridine resulted in the complete recovery of the starting material. When the alcohol **99** was treated with potassium hydride and carbon disulfide in tetrahydrofuran at room temperature followed by addition of an excess of methyl iodide, the S-methyl xanthate **106** was furnished as a single reaction product in 40% yield. Neither changing the solvent to 1,2-dimethoxyethane[86] nor use of imidazole as a catalyst[79] in the



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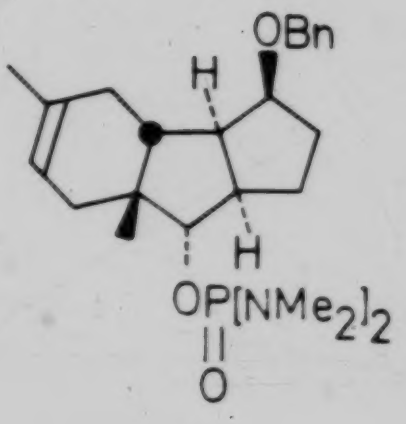

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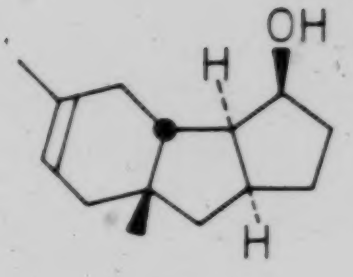

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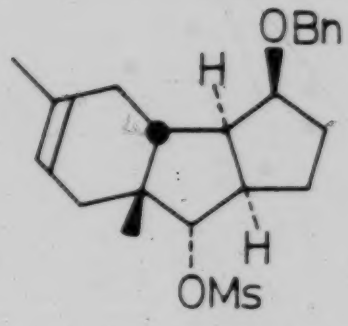

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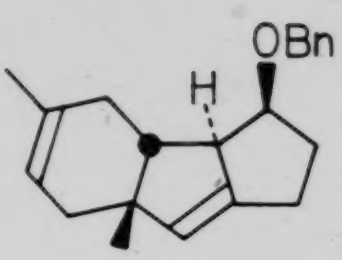

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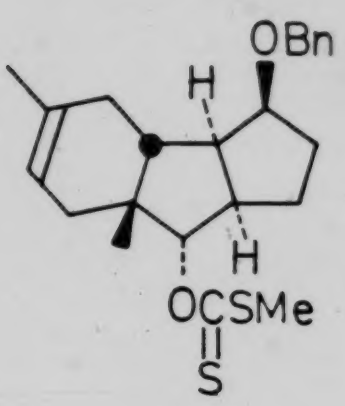


106

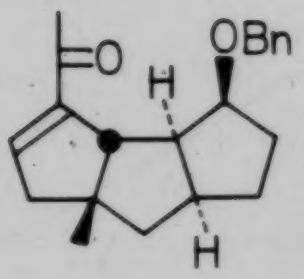
reaction resulted in the improvement of the yield. The structure of the xanthate **106** was evident from its spectral data. In the proton NMR spectrum, the doublet at δ 5.69 (J = 7 Hz) corresponded to the proton adjacent to the xanthate while the S-methyl group gave a sharp singlet at δ 2.66. The chemical ionization mass spectrum showed the molecular ion at 402, equivalent to the molecular formula $C_{23}H_{30}O_2S_2$. Heating the xanthate **106** with tri-n-butylstannane and a catalytic amount of 2,2'-azobis[2-methyl-2-propionitrile] in toluene at reflux for 2 h gave the compound **82** in quantitative yield. Though the xanthate pathway (**99** → **106** → **82**) did not result in a significant increase in the yield of **82** over the mesylate pathway (**99** → **104** → **82**), the former pathway furnished the compound **82** as a single product and thus avoided the tedious purification step encountered in the reduction of the mesylate **104**.

After the diol **78** was successfully converted to the compound **82**, we focused our attention on the modification of the cyclohexene ring of **82**. Previously, in a one-pot reaction, the diacetate **83** was efficiently converted to the triquinanoid comound **84** involving an ozonolysis-reduction-aldol condensation process (vide supra). It was expected that application of this method to the compound **82** would produce the enone **107**. Accordingly, a dichloro-

methane solution of the compound **82** was saturated with ozone at -78°C. Reduction of the ozonide thus formed with dimethyl sulfide directly gave the enone **107** in 60% yield. The IR spectrum of this compound showed two absorption bands at 1660 and 1614 cm^{-1} corresponding to the enone carbonyl and the carbon-carbon double bond respectively. In the proton NMR spectrum, the olefinic proton appeared as a broad singlet at δ 6.69. The acyl methyl group gave a singlet at δ 2.32. The mass spectrum registered a molecular ion peak at 310.1932 equivalent to the molecular formula $C_{21}H_{26}O_2$.

The conversion of the enone **107** to the target molecule requires two major operations - the construction of the gem-dimethyl group at C-1 (capnellane numbering) and the introduction of the exo-methylene group at C-9. The former operation could, in principle, be carried out by first effecting the deconjugative α-methylation[87,88,89] of the enone **107** to produce the ketone **108**. Oxidation of the acyl group of **108** followed by reduction of the ester group of the resulting compound **109** to the corresponding alkane should complete the construction of the required gem-dimethyl group. In accordance with the above strategy, the enone **107** was treated with potassium t-butoxide in tetrahydrofuran at 0°C. Addition of an excess of methyl iodide to the reaction mixture resulted in the

consumption of the starting material in less than 5 min. The proton NMR spectrum of the crude reaction product showed no signal for the acyl methyl group at δ 2.32 but showed two broad singlets, integrating for a total of one proton, at δ 6.58 and 6.44. These NMR data indicated that the α,β-unsaturated ketone carbonyl of **107** was selectively alkylated at the α' position. Conceivably, this problem could be avoided by converting the enone **107** to the ester **110** which then could be subjected to the deconjugative α-methylation reaction. The ester **110** could, in principle, be obtained by subjecting the ketone **107** to the haloform reaction.[90] Treatment of the ketone **107** with an excess of sodium methoxide in methanol at 0°C followed by the addition of three equivalents of iodine gave the ester **110** in 45% yield. Its IR spectrum showed an intense carbonyl absorption at 1717 cm^{-1}. The proton NMR spectrum showed the olefinic proton at δ 6.62 as a broad singlet. The carbomethoxy group gave a sharp singlet at δ 3.78. The mass spectrum of this compound showed a molecular ion peak at 326.1885 corresponding to the molecular formula $C_{21}H_{26}O_3$. To effect the deconjugative methylation, the ester **110** was treated with a preformed complex of lithium diisopropylamide and hexamethylphosphoramide (1:1 ratio)[91] in tetrahydrofuran at 0°C and an excess of methyl iodide. However, the starting material was recovered unchanged.



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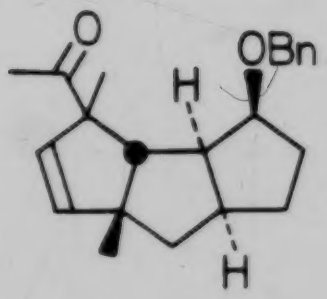

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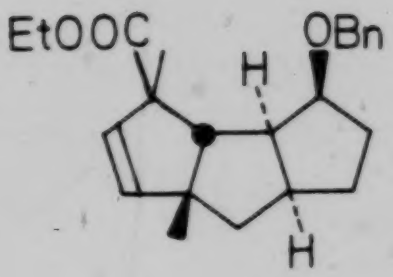

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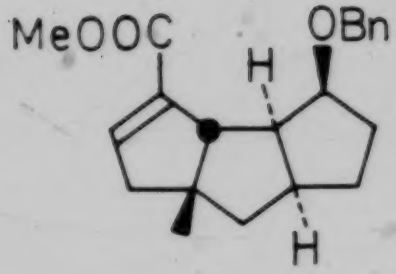

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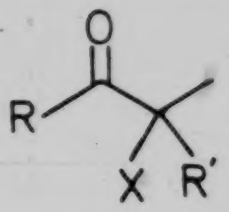

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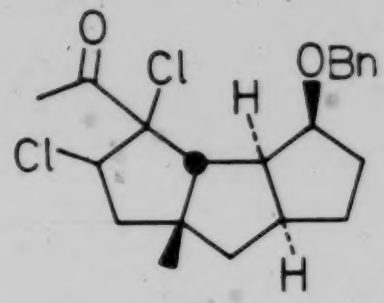

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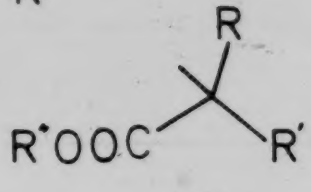
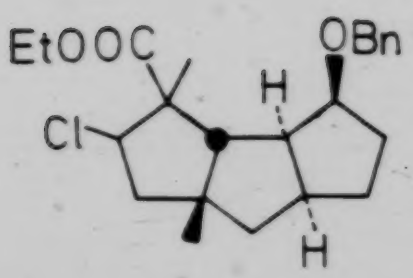


112

For a long time it has been known that the Favorskii rearrangement[92] of α-halo methyl ketones like **111** could be effected under basic conditions to produce the corresponding α-methyl acids or esters of the type **112**. It was conceivable that the dichloride **113** prepared from the enone **107** could undergo the Favorskii rearrangement to give either the ester **109** or **114**. Towards this end, the enone **107** was treated with a saturated solution of chlorine in dichloromethane at 0°C. The resulting dichloride **113**, without any purification, was refluxed with sodium ethoxide in ethanol for 3 h to effect the Favorskii rearrangement. The mass spectrum of the product showed a molecular ion peak at 354.2184 equivalent to the molecular formula $C_{23}H_{30}O_3$ required for the desired compound **109**. The proton NMR spectrum, however, showed a sharp singlet at δ 5.58 integrating for one proton only. This suggested that the product was not the desired compound **109** but was probably the isomeric compound **115**. The presence of an intense absorption band at 1711 cm^{-1} in the IR spectrum corroborated well with this latter structure. Presumably the ring opening of the intermediate cyclopropane **116** as depicted, followed by the isomerization of the carbon-carbon double bond leads to the formation of the compound **115**. This type of ring opening has previously been observed.[93,94]

It was realized that the construction of the required gem-dimethyl group could as well be achieved via the ketone **117**. In an attempt to prepare this ketone, the enone **107** was subjected to the Baeyer-Villiger oxidation[95,96,97] using m-chloroperbenzoic acid in dichloromethane at 0°C. However a complex mixture of products was formed. On the other hand, treatment of the enone with hydroxylamine hydrochloride in methanol in the presence of anhydrous sodium acetate[98] gave the oxime **118** in quantitative yield. This α,β-unsaturated oxime should, in principle, undergo the Beckmann rearrangement under various conditions[98,99,100,101] to furnish the ketone **117**. Accordingly, by treating the oxime **118** with phosphorus oxychloride[98] in pyridine-triethylamine (1:1 ratio) and by hydrolyzing the reaction mixture with aqueous hydrochloric acid, the ketone **117** was obtained in 70% yield. Its IR spectrum showed a carbonyl absorption at 1725 cm^{-1}. The proton NMR spectrum showed a singlet at δ 1.18 for the angular methyl group and a multiplet for the benzyloxymethine proton at δ 3.89. The mass spectrum showed a molecular ion peak at 284.1773 corresponding to the molecular formula $C_{19}H_{24}O_2$.

The ketone carbonyl of the compound **117** could, in principle, be transformed into the desired gem-dimethyl moiety by a three step sequence comprising of its



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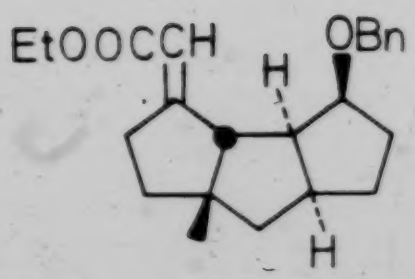

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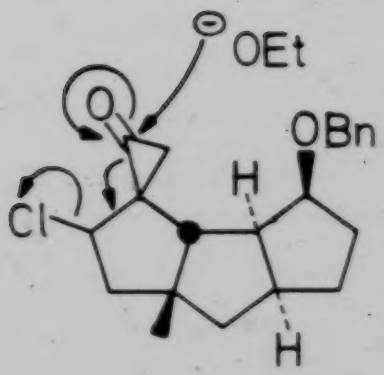

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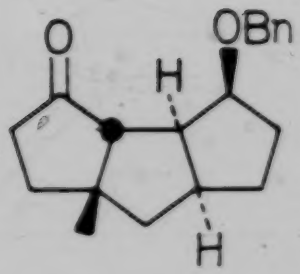

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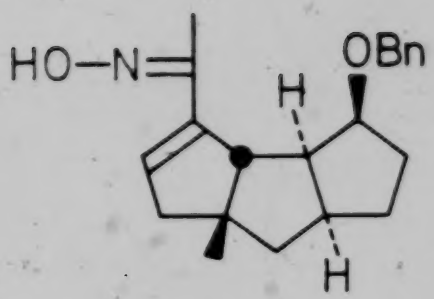

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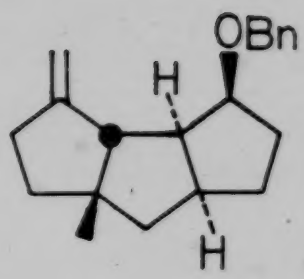


119

conversion to the corresponding methylidene derivative, cyclopropanation and the hydrogenolysis of the resulting cyclopropane. For the preparation of the methylidene compound **119** from the ketone **117**, the Wittig reaction[102] was used because of its simplicity, although many other methods[103,104,105,106] are available for this purpose. Refluxing the ketone **117** in benzene with methylenetriphenylphosphorane, generated in situ from potassium t-butoxide[107] and methyltriphenylphosphonium bromide, furnished the expected compound **119** in 80% yield. Its IR spectrum showed weak absorption bands at 1650 and 880 cm^{-1}, characteristic of a terminal olefin. The proton NMR showed two multiplets at δ 4.88 and 4.82 for the olefinic protons, a sharp singlet at δ 1.06 for the angular methyl group and a multiplet at δ 3.85 for the benzyloxymethine proton. The mass spectrum displayed a molecular ion peak at 282.1974 equivalent to the molecular formula $C_{20}H_{26}O$.

The cyclopropanation of isolated carbon-carbon double bonds with zinc-copper couple and methylene iodide was originally demonstrated by Simmons and Smith.[108] In the ensuing years, several modifications of the Simmons-Smith reaction[109,110,111,112,113] have been developed. Of all these modifications, the procedure involving the heating of an olefinic compound with diethylzinc and methylene iodide in benzene in the presence of air has been

reported[111,112,113] to provide the corresponding cyclopropane in excellent yield. Accordingly, the olefin **119** was heated with an excess of diethylzinc and methylene iodide in benzene at 50°C in the presence of air. The cyclopropyl derivative **120** was obtained in 80% yield. The proton NMR spectrum of this compound showed two multiplets at δ 0.35 and 0.55, each integrating for two cyclopropyl protons. The angular methyl group gave a sharp singlet at δ 1.20. Although the molecular ion could not be detected in the mass spectrum, the fragment at m/e 205.1589, resulting from the loss of the benzyl unit, was registered.

It is known that the hydrogenolysis of a cyclopropane with palladium-charcoal[114,115] or platinum black[116,117] results in the cleavage of the least substituted bond of the cyclopropane ring. It has also been demonstrated that the benzyl group could be cleaved under similar conditions.[118,119] On the basis of these findings it was expected that the alcohol **123** could directly be obtained by the hydrogenolysis of the cyclopropyl derivative **120**. Accordingly, the compound **120** was subjected to hydrogenolysis with 5% palladium on charcoal in glacial acetic acid at room temperature under two atmospheres of hydrogen. The IR spectrum of the resulting product showed a hydroxyl absorption at 3410 cm^{-1} indicating that the

benzyl ether was cleaved. However, the proton NMR spectrum showed a complex multiplet between δ 0.60 and 0.32, integrating for a total of four protons, indicating that the cyclopropane ring was intact. This was confirmed by the mass spectrum which registered a molecular ion at 206.1661 corresponding to the molecular formula $C_{14}H_{22}O$ required for the alcohol **121**. Alternatively, the hydrogenolysis of **120** was attempted with platinum black under the same conditions as above. The resulting compound showed no hydroxyl absorption in the IR spectrum. The proton NMR spectrum showed no signals corresponding to the benzyl group. However, it showed two doublet of doublets at δ 3.22 and 3.07 (J = 6 Hz and J' = 9 Hz each) each integrating for one proton. This spectral data suggested that the hydrogenation rather than hydrogenolysis of the benzyl group had taken place. The presence of two multiplets at δ 0.57 and 0.30, each integrating for two protons, indicated that the cyclopropane ring was not hydrogenolyzed under these conditions as well. On the basis of these observations the structure **122** was assigned to the product. This structural assignment was confirmed by the mass spectrum which displayed a molecular ion peak at 302.2631 corresponding to the molecular formula $C_{21}H_{34}O$ of the compound **122**. It has been observed[118,120] previously that when platinum is used

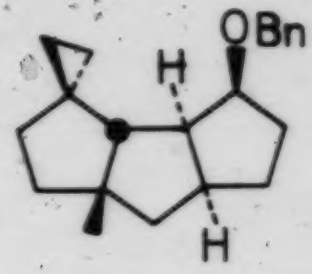
as a catalyst, benzyl group occasionally undergoes hydrogenation rather than hydrogenolysis. To circumvent this problem, the hydrogenation of the alcohol **121** with platinum in glacial acetic acid under two atmospheres of hydrogen was attempted. To our delight, the desired alcohol **123** was obtained in quantitative yield. Its IR spectrum showed the hydroxyl absorption at 3410 cm^{-1}. The proton NMR showed a multiplet at δ 4.12 for the hydroxymethine proton. Three singlets at δ 1.22, 1.06 and 0.98 corresponded to three methyl groups. The mass spectrum registered a molecular ion at 208.1827 equivalent to the molecular formula $C_{14}H_{24}O$.

When the alcohol **123** was subjected to oxidation with pyridinium chlorochromate in dichloromethane at room temperature, the known ketone **13**[9,12,16,17,18] was isolated in 80% yield. The IR spectrum showed an intense carbonyl absorption at 1737 cm^{-1}. The proton NMR spectrum displayed three singlets at δ 1.10, 1.06 and 0.96 for three methyl groups. The mass spectrum registered a molecular ion peak at 206.1670 equivalent to the molecular formula $C_{14}H_{22}O$.

Finally, treatment of the ketone **13** with methylenetriphenylphosphorane, generated <u>in situ</u> from methyltriphenylphosphonium bromide and potassium-<u>t</u>-butoxide,[107] in refluxing benzene gave (±)$\Delta^{9(12)}$-capnellene (**2**) in 75%

yield. Its IR spectrum showed a weak absorption band at 870 cm^{-1} for the terminal double bond. The proton NMR spectrum showed two broad singlets at δ 4.90 and 4.80 for the olefinic protons and three sharp singlets at δ 1.16, 1.06 and 0.98 for three methyl groups. The carbon-13 NMR spectrum displayed signals at δ 159.00, 104.99, 69.16, 53.34, 52.34, 48.00, 46.05, 41.73, 40.62, 31.84, 31.60, 30.85, 29.13 and 26.09. The mass spectrum registered the molecular ion peak at 204.1867 equivalent to the molecular formula $C_{15}H_{24}$ of (±)$\Delta^{9(12)}$-capnellene (**2**). These spectral data are in good agreement with those reported[5,11] for $\Delta^{9(12)}$-capnellene (**2**).

The synthesis of $\Delta^{9(12)}$-capnellene was achieved in twenty-four steps. The purpose of devising a general and flexible strategy for the synthesis of capnellanoids was achieved by the successful preparation of the intermediates **99** and **107** which could conceivably be converted to other capnellanoids.



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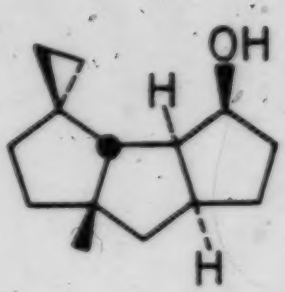
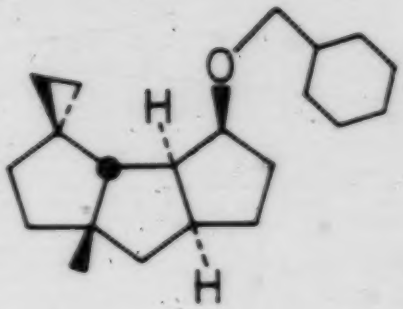
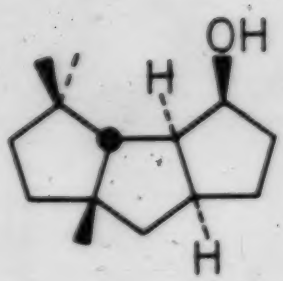


121



122



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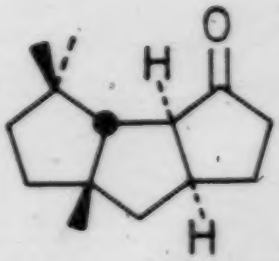

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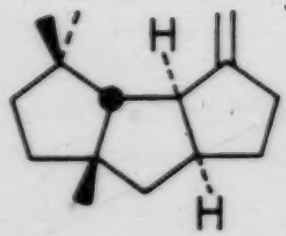

2

EXPERIMENTAL

General

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Elemental analyses were performed by the microanalytical laboratory of this department. Infrared spectra (IR) were recorded on a Nicolet 7-199 FT-IR spectrophotometer and were obtained on neat samples unless otherwise stated. The proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Varian HA-100/Digilab, Bruker W-200 or Bruker W-400 spectrometers and were obtained on solutions in deuterochloroform with tetramethylsilane as the internal reference. Carbon-13 nuclear magnetic resonance spectra (carbon-13 NMR) were recorded on a Bruker W-200 and Bruker W-400 spectrometer and were obtained on deuterochloroform solutions with tetramethylsilane as internal reference. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and b = broad. Mass spectra (MS) were recorded on a A.E.I. model MS 9, MS 12 or MS 50 mass spectrometer.

Materials

Benzene, toluene and ether were freshly distilled over lithium aluminium hydride. Tetrahydrofuran was freshly distilled over sodium in the presence of benzophenone. Dichloromethane used for the reaction purpose was freshly distilled over calcium hydride. 1,1-Diethoxyethene,[26] 2-cyclopentenone[28] and phenyl chlorothionocarbonate[81] were prepared according to the literature procedures. Argon was purified by passing through a train of gas wash bottles containing sequentially, Fieser's solution,[121] concentrated sulfuric acid and potassium hydroxide pellets.

(1R*,5R*)-6,6-Diethoxybicyclo[3.2.0]heptan-2-one (64)*

The apparatus used for the photocycloaddition is shown diagramatically in Fig. 1. The reaction vessel was charged with 2-cyclopentenone (59) (1 g, 12.2 mmol), 1,1-diethoxyethene (14 g, 122 mmol) and benzene (50 mL). This mixture was agitated throughout the reaction period by passing a steady flow of argon gas through it. After cooling the reaction mixture to approximately 10°C with ice and water, it was irradiated with a 450 W Hanovia

* The stereochemical designation used for all the chemical names in this section denote relative stereochemistry. All compounds used and obtained were racemic.

medium pressure mercury vapour lamp using a Pyrex filter. After 24 h benzene was removed under reduced pressure. Excess 1,1-diethoxyethene was removed by distillation at 70°C/20 Torr. Bulb-to-bulb distillation (80°C*/0.8 Torr) of the residue gave pure photoadduct **64** (2 g, 85%) as a colorless oil: IR 1740 cm^{-1} (five membered C=O); H^1 NMR δ 3.39, 3.40, (both q, 1H each, J = 7 Hz each, $-O-CH_2-CH_3$), 3.45, 3.46 (both q, 1H each, J = 7 Hz each, $-O-CH_2-CH_3$), 1.18, 1.21 (both t, 3H each, J = 7 Hz each, 2 x $-O-CH_2-CH_3$); MS M^+ 198.1254 (calcd. for $C_{11}H_{18}O_3$: 198.1256).

(1R*,2S*,5R*)-6,6-diethoxybicyclo[3.2.0]heptan-2-ol (**65**)

A solution of the photoadduct **64** (2 g, 10.1 mmol) in tetrahydrofuran (20 mL) was cooled to 0°C. To this was added lithium tri-t-butoxyaluminohydride (3.1 g, 12.1 mmol). The resulting turbid reaction mixture was stirred at room temperature under the argon atmosphere for 6 h.

The reaction mixture was concentrated and the residue was decomposed with a saturated aqueous ammonium chloride solution. The precipitate was filtered off and was washed exhaustively with ether. The combined ether layer was washed with water and saturated sodium chloride solution,

* In all the bulb-to-bulb distillations, the temperature mentioned is the oven temperature.

dried over anhydrous sodium sulfate and concentrated. Bulb-to-bulb distillation (95°C/0.8 Torr) of the crude product thus obtained, gave pure alcohol **65** (2.0 g, quantitative yield): IR 3440 cm^{-1}; ^1H NMR δ 4.25 (m, 1H, -CHOH-), 3.39, 3.40 (both q, 2H each, J = 7 Hz each, 2 x -O-CH_2-CH_3), 1.14, 1.26 (both t, 3H each, J = 7 Hz each, 2 x -O-CH_2-CH_3); MS M^+ 200.1366 (calcd. for $C_{11}H_{20}O_3$: 200.1412).

(1R*,2S*,5R*)-2-Benzyloxy-6,6-diethoxybicyclo[3.2.0]-heptane (**66**)

A 50 mL round bottomed flask was charged with sodium hydride (50% dispersion in oil, 0.6 g). This was freed from mineral oil by washing it with tetrahydrofuran (3 x 10 mL). A suspension of this oil free sodium hydride in tetrahydrofuran (10 mL) was cooled to 0°C. A solution of the alcohol **66** (2 g, 10.1 mmol) in tetrahydrofuran (10 mL) was added dropwise to the cooled suspension of sodium hydride. After stirring the resulting solution under argon atmosphere for 15 min, benzyl bromide (2.1 g, 1.45 mL, 12.3 mmol) was added in a dropwise fashion. The resulting light brown solution was stirred overnight at room temperature. The reaction mixture was diluted with ether (150 mL), washed successively with water and saturated brine solution, dried over anhydrous sodium

sulfate and concentrated. Column chromatography of the residue on silica gel, eluting with dichloromethane, gave the pure product **66** (2.67 g, 92% yield): ^{1}H NMR δ 7.30 (s, 5H, aromatic), 4.20, 4.21 (both s, 1H each, -O-C**H**$_2$-Ph), 3.94 (m, 1H, -O-C**H**-), 3.38, 3.39 (both q, 2H each, J = 7 Hz each, 2 x -O-C**H**$_2$-CH$_3$), 1.17, 1.19 (both t, 3H each, J = 7 Hz each, 2 x -O-CH$_2$-C**H**$_3$); MS m/e 245.1539 (M^+-45; calcd. for $C_{16}H_{21}O_2$: 245.1542).

(1R*,2S*,5R*)-2-Benzyloxybicyclo[3.2.0]heptan-6-one (**67**)

To a stirred solution of the benzyl ether **66** (2.6 g, 9 mmol) in tetrahydrofuran (40 mL), was added a solution of oxalic acid (3 g) in water (15 mL) at room temperature. The resulting mixture was stirred overnight at room temperature. The reaction mixture was poured into ether (200 mL). The organic layer was washed successively with water, saturated sodium bicarbonate solution, water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Bulb-to-bulb distillation (126°C/0.075 Torr) gave pure cyclobutanone **67** (1.93 g, quantitative yield): IR 1770 cm^{-1} (four membered C=O); ^{1}H NMR δ 7.30 (s, 5H, aromatic), 4.54 (s, 2H, -O-C**H**$_2$-Ph), 4.16 (m, 1H, -O-C**H**-); MS M^+ 216.1158 (calcd. for $C_{14}H_{16}O_2$: 216.1150).

Anal. calcd for $C_{14}H_{16}O_2$: C, 77.67; H, 7.45. Found: C, 77.20; H, 7.43.

(1R*,3S*,5R*,6S*)-6-Benzyloxy-3-carboethoxybicyclo[3.3.0]-octan-2-one (68)

To a stirred solution of the cyclobutanone 67 (2.2 g, 10.2 mmol) in ether (30 mL) cooled to 0°C, was added freshly distilled boron trifluoride etherate (1.74 g, 1.5 mL, 12.2 mmol). After stirring for 20 min, a solution of ethyl diazoacetate (1.4 g, 12.2 mmol) in ether (10 mL) was added over a period of 30 min. The resulting orange-brown reaction mixture was stirred overnight under the argon atmosphere. The reaction mixture was diluted with ether and was washed successively with saturated sodium bicarbonate solution, water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Bulb-to-bulb distillation (140°C/0.05 Torr) gave the product as a colorless oil (2.45 g, 80%): IR 1750 (five-membered C=O), 1723 (ester C=O), 1660 (α,β-unsaturated ester C=O) and 1620 cm^{-1} (C=C); ^1H NMR δ 7.26-7.34 (complex, 5H, aromatic), 4.34-4.56 (complex, 2H, $PhCH_2$-O-), 4.14-4.22 (complex, 2H, -O-CH_2-CH_3), 1.22-1.30 (complex, 3H, -O-CH_2-CH_3); carbon-13 NMR δ 214.61, 213.25, 211.97, 175.35, 169.72, 169.52, 169.05, 138.47, 138.31, 138.22, 128.17, 127.91, 127.73, 127.62, 127.37, 127.29,

127.05, 126.91, 100.22, 81.86, 81.61, 81.54, 81.00, 80.92, 71.49, 71.39, 71.29, 71.21, 70.65, 70.52, 62.41, 60.96, 60.93, 60.86, 59.65, 59.50, 55.42, 55.10, 50.87, 49.37, 47.66, 43.48, 43.37, 42.86, 42.82, 40.08, 38.17, 38.03, 37.82, 31.67, 31.13, 30.74, 29.55, 29.47, 29.17, 29.05, 28.91, 28.09, 25.60, 25.54, 25.32, 24.78, 24.55, 24.22, 14.19, 13.98; MS M^+ 302.1511 (calcd. for $C_{18}H_{22}O_4$: 302.1513).

Anal. calcd. for $C_{18}H_{22}O_4$: C, 71.52; H, 7.28. Found: C, 71.67; H, 7.36.

(1R*,5R*,6S*)-6-Benzyloxy-3-carboethoxybicyclo[3.3.0]oct-3-en-2-one (**70**).

a) Using selenium dioxide

A mixture of the impure keto-ester **68** (0.3 g) and senenium dioxide (0.33 g, 3 mmol) in t-butyl alcohol containing 5% glacial acetic acid was heated at 75°C for 6 h under the argon atmosphere. The resulting dark red solution was poured in water (10 mL). The aqueous layer was extracted with ether. The combined ether extract was washed with water and saturated brine solution, dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with dichloromethane, gave pure compound **70** (0.065 g, 20% yield): IR 1740 (five-membered C=O), 1720 (ester C=O) and 1620 cm^{-1} (C=C); ^1H

NMR δ 8.40 (d, 1H, J = 4 Hz, -CH=C-), 7.39 (s, 5H, aromatic), 4.58, 4.65 (AB q, 2H, J = 12 Hz, $PhCH_2$-O-), 4.29, 4.31 (both q, 1H each, J = 7 Hz each, -O-CH_2-CH_3), 4.10 (ddd, 1H, J = 7 Hz, J' = 8 Hz, J" = 10.5 Hz, -O-CH-), 3.50 (ddd, 1H, J = 3 Hz, J' = 6 Hz, J" = 9 Hz, -CH-C=C-), 2.82 (ddd, 1H, J = 2 Hz, J' = 6 Hz, J" = 9 Hz, -CH-CO-), 1.35 (t, 3H, J = 7 Hz, -OCH_2-CH_3); carbon-13 NMR δ 205.63, 171.16, 16.43, 138.24, 137.82, 128.39, 127.74, 127.41, 126.80, 80.50, 72.08, 65.72, 60.85, 49.09, 46.03, 28.55, 24.58; MS M^+ 300.1366 (calcd. for $C_{18}H_{20}O_4$: 300.1362).

b) Using DDQ

A solution of the keto-ester **68** (0.2 g), and ddq (0.25 g, 1.25 mmol) in benzene (5 mL) was refluxed under argon atmosphere for 2 h. On cooling, the reaction mixture was diluted with ether and was washed with water and saturated brine solution. The organic layer was dried over anhydrous sodium sulfate and concentrated. Chromatography of the residue on silica gel column, eluting with dichloromethane, gave pure compound **70** (0.03 g, 15% yield).

c) Using the phenylselenenyl chloride method

A solution of the keto-ester **68** (10 g) in tetrahydrofuran (200 mL) at 0°C, was treated under the argon atmo-

sphere with sodium hydride (50% dispersion in oil; 2.0 g, 41.7 mmol). The resulting brown solution was stirred for 30 min. A solution of phenylselenenyl chloride (8 g, 1.3 mmol) in tetrahydrofuran (50 mL) was added over a period of 20 min. After stirring this reaction mixture at room temperature for 2 h, the solvent was removed under reduced pressure. The residue was taken up in ether and washed with water. The ether layer was dried over anhydrous sodium sulfate and concentrated. The crude selenide **71** thus obtained was redissolved in dichloromethane (400 mL). This vigorously stirred solution was cooled to 0°C and an aqueous solution of hydrogen peroxide (30%; 10 mL) was added in three portions. Within a short time the temperature of the reaction mixture rose to 30°C and the color of the reaction mixture changed from deep red to light yellow. The reaction mixture was stirred further for 30 min. The organic layer was throughly washed with water, saturated sodium carbonate and finally with saturated brine solution. The organic layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with dichloromethane, gave the pure product (6 g, 60%).

(1R*,3S*,8R*,9R*,10S*)-10-Benzyloxy-3-carboethoxy-6-methyltricyclo[7.3.0.0^{3,8}]dodec-5-en-2-one (**76**)

A three-neck 1-L round-bottomed flask, equipped with a mechanical stirrer, was charged with the enone-ester **70** (20 g, 67 mmol), isoprene (270 g, 400 mL, 4 mol), and ether (100 mL). Vigorous stirring was started and the mixture was cooled to -78°C. Anhydrous stannic chloride (21 g, 9.4 mL, 72 mmol) was added slowly over a period of 30 min. The resulting yellow reaction mixture was stirred under the argon atmosphere for 10 h at -78°C. The reaction mixture was poured into saturated sodium carbonate solution. The precipitate was filtered and was washed thoroughly with ether. The combined organic filtrate was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Column chromatography on silica gel column, eluting initially with dichloromethane and then with 7% ether in dichloromethane, gave pure Diels-Alder adduct **76** (14.8 g, 60% yield). On recrystallization from hexane, white crystals of **76**, m.p. 68-69°C, were obtained. This compound showed, IR ($CHCl_3$ cast) 1748 (five-membered C=O) and 1725 cm^{-1} (ester C=O); ^1H NMR δ 7.30 (s, 5H, aromatic), 5.44 (bs, 1H, -CH=C-), 4.64, 4.54 (ABq, J = 13 Hz each, $PhCH_2$-O-), 4.19, 4.21 (both q, 1H each, J = 7 Hz each, -O-CH_2-CH_3), 4.04 (m, 1H, -O-CH-), 1.68 (bs, 3H,

CH_3-C=), 1.34 (t, 3H, J = 7 Hz, -O-CH_2-CH_3); carbon-13 NMR δ 214.31, 170.34, 138.11, 131.58, 127.69, 126.81, 126.60, 126.42, 116.07, 81.62, 71.33, 60.55, 59.39, 47.51, 43.20, 35.64, 28.96, 28.13, 24.88, 24.16, 23.19.

Anal. calcd. for $C_{23}H_{28}O_4$: C, 75.00; H, 7.60. Found: C, 75.08; H, 7.64.

(1R*,3R*,8R*,9R*,10S*)-10-Benzyloxy-3-carboethoxy-6-methylspiro[tricyclo-[7.3.0.0^{3,8}]dodec-2-en-5-one[2,1']-2',5'-dithiacyclopentane] (77)

To a stirred solution of the Diels-Alder adduct 76 (0.15 g, 0.4 mmol) in dichloromethane (5.0 mL) under the argon atmosphere was added boron trifluoride etherate (0.07 g, 0.06 mL, 0.5 mmol) at room temperature. To this complex was added 1,2-ethanedithiol (0.05 g, 0.045 mL, 0.53 mmol). The resulting reaction mixture was stirred for 15 min. It was diluted with dichloromethane and washed with saturated sodium carbonate solution, water and saturated brine solution. The organic layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 2% ether in dichloromethane, gave pure product 77 (0.08 g, 45% yield): IR 1722 cm^{-1} (ester C=O); ^1H NMR δ 7.36 (s, 5H, aromatic), 5.33 (bd, 1H, J = 4 Hz, -CH=C-), 4.65, 4.52 (ABq, 1H each, J = 12 Hz each, PhCH_2-O-), 4.14 (q, 2H, J =

7 Hz, -O-C**H**$_2$-CH$_3$), 3.90 (m, 1H, -O-C**H**-), 3.06-3.32 (m, 4H, -S-CH$_2$-CH$_2$-S-), 1.64 (bs, 3H, CH$_3$-C=C-), 1.28 (t, 3H, J = 7 Hz, -O-CH$_2$-C**H**$_3$); MS M$^+$ 444.1794 (calcd. for $C_{25}H_{32}O_3S_2$: 444.1793).

(1R*,2S*,3R*,8R*,9R*,10S*)-10-Benzyloxy-2-hydroxy-3-hydroxymethyl-6-methyltricyclo[7.3.0.0^{3,8}]dodec-5-ene (78)

The stirred solution of the adduct **76** (10 g, 27 mmol) in tetrahydrofuran (200 mL) cooled to 0°C was treated with a solution of SMEAH (14.7 mL of 3.4 M, 50 mmol) in tetrahydrofuran in a drop-wise fashion. The resulting reaction mixture was stirred under the argon atmosphere for 6 h at room temperature. The solvent was removed under reduced pressure and the residue was decomposed with a saturated solution of ammonium chloride. The precipitate was filtered off and was thoroughly washed with ether. The combined organic filtrate was washed with water and saturated brine solution. The organic layer was dried over anhydrous sodium sulfate and concentrated. The solid compound obtained was purified on silica gel column, eluting with 20-50% ether in dichloromethane, to give pure diol **78** (8.9 g, quantitative yield). On recrystallization from dichloromethane hexane, white crystals of **78**, mp 136-137°C, were obtained: IR 3360 cm^{-1}; ^{1}H NMR δ 7.30 (s, 5H, aromatic), 5.40 (bs, 1H, -CH=C-), 4.59, 4.49 (ABq, 1H

each, J = 12 Hz each, $-PhCH_2-O$), 3.83 (m, 1H, $-O-\underset{|}{C}H-$), 3.70, 3.50 (ABq, 1H each, J = 10 Hz each, $-CH_2-OH$), 3.72 (d, 1H, J = 7 Hz, $-\underset{|}{C}H-OH$), 1.66 (bs, 3H, $CH_3-\underset{|}{C}=$); MS M^+ 328.2041 (calcd. for $C_{21}H_{28}O_3$: 328.2043), m/e 310.1930 (M^+-18; calcd. for $C_{21}H_{26}O_2$: 310.1933), m/e 292.1824 (M^+-36; calcd. for $C_{21}H_{24}O$: 292.1827).

Anal. calcd. for $C_{21}H_{28}O_3$: C, 76.78; H, 8.59. Found: C, 76.96; H, 8.57.

(1R*,2R*,3R*,8R*,9R*,10S*)-10-Benzyloxy-2-hydroxy-3-hydroxymethyl-6-methyltricyclo[7.3.0.0^{3,8}]dodec-5-ene (**81**)

A solution of potassium tri-s-butylborohydride (3.5 mL of 1 M, 3.5 mmol) was added to a stirred solution of the Diels-Alder adduct **76** (1 g, 3 mmol) in tetrahydrofuran (10 mL) at 0°C. The resulting orange-red reaction mixture was stirred under argon atmosphere for 6 h at room temperature. It was treated with aqueous sodium hydroxide (1 N, 5 mL) and aqueous hydrogen peroxide (30%, 1 mL). The resulting light yellow solution was stirred for 60 min. The reaction mixture was extracted with ether and the combined ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated to yield the crude alcohol **80** (0.95 g).

The crude alcohol **80** (0.95 g) was redissolved in tetrahydrofuran (5 mL) and cooled to 0°C. This cold solution was treated with SMEAH (3.5 mL of 3.4 M, 11.5 mmol). The resulting reaction mixture was stirred under argon atmosphere for 6 h at room temperature. The reaction mixture was concentrated and the residue was decomposed with saturated aqueous ammonium chloride solution. The precipitate was filtered off and washed thoroughly with ether. The combined ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 20-40% ether in dichloromethane, gave pure diol **81** (0.72 g, 80% yield). Recrystallization from dichloromethane-hexane gave white crystals of the diol **81**, mp 110-111°C: IR 3360 cm^{-1}; ^1H NMR δ 7.30 (s, 5H, aromatic). 5.30 (bs, 1H, -CH=C-), 4.65, 4.49 (ABq, 1H each, J = 12 Hz, Ph-C**H**$_2$-O-), 3.83 (m, 1H, -O-C**H**-), 3.66, 3.57 (ABq, 1H each, J = 11 Hz, -C**H**$_2$-OH), 3.65 (d, 1H, J = 6 Hz, -C**H**-OH), 1.66 (bs, 3H, C**H**$_3$-C=C-); MS M^+ 328.2041 (calcd. for $C_{21}H_{28}O_3$: 328.2044), m/e 310.1930 (M^+-18; calcd. for $C_{21}H_{26}O_2$: 310.1933), m/e 292.1819 (M^+-36, calcd. for $C_{21}H_{24}O$: 292.1827).

Anal. calcd. for $C_{21}H_{28}O_3$: C, 76.78; H, 8.59. Found: C, 76.60; H, 8.50.

(1R*,2S*,3R*,8R*,9R*,10S*)-2-Acetoxy-3-acetoxymethyl-10-benzyloxy-6-methyltricyclo[7.3.0.0^{3,8}]dodec-5-ene (**83**)

A mixture of the diol **78** (200 mg, 0.6 mmol), acetic anhydride (3.0 mL) and pyridine (2.0 mL) was heated under argon atmosphere at 80°C for 30 min. The reaction mixture was poured into water and extracted with ether. The combined ether extract was washed with water, saturated sodium carbonate solution, dilute hydrochloric acid and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with dichloromethane gave pure diacetate **83** (0.25 g, 97% yield): IR 1740 cm^{-1} (acetate C=O); ^{1}H NMR δ 7.34 (s, 5H, aromatic), 5.31 (bs, 1H, -CH=C-), 4.78 (d, 1H, J = 6 Hz, -CH-OAC), 4.60, 4.49 (ABq, 1H each, J = 9 Hz, each, Ph-CH$_2$-O-), 3.84, 3.89 (ABq, 1H each, J = 9 Hz, -CH$_2$-OAc), 3.82 (m, 1H, -O-CH-), 2.05, 2.03 (both s, 3H each, 2 x -O-CO-CH$_3$), 1.66 (s, 3H, CH$_3$-C=); CIMS (M+NH$_4^{\oplus}$) 430.00; MS m/e 352.2035 (M$^+$-60; calcd. for $C_{23}H_{28}O_3$: 352.2038).

(1S*,2R*,3R*,7S*,8S*,9S*)-2-Acetoxy-3-acetoxymethyl-6-acetyl-9-benzyloxytricyclo[6.3.0.0^{3,7}]undec-5-ene (**84**)

The diacetate **83** (200 mg, 0.5 mmol) was dissolved in dichloromethane (5 mL) and cooled to -78°C. Ozone was

passed through this solution until the blue color of ozone persisted. The flow of ozone was stopped, the solution was purged with argon to remove excess ozone, and dimethyl sulfide (5 mL) was added to this colorless solution. The resulting mixture was stirred overnight under argon atmosphere at room temperature. The reaction mixture was diluted with ether and washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 0-2% ether in dichloromethane, gave pure enone **84** (122 mg, 60% yield): IR 1740 (acetate C=O), 1660 cm^{-1} (α,β-unsaturated ketone C=O); ^1H NMR δ 7.39-7.26 (m, 5H, aromatic), 6.60 (bs, 1H, $\underline{CH}=\underline{C}$-), 5.36 (d, 1H, J = 8 Hz -$\underline{CH}$-OAc), 4.67, 4.51 (ABq, 1H each, J = 12 Hz each, PhCH_2-O-), 3.97 (m, 1H, -O-$\underline{CH}$-), 3.94, 3.92 (both s, 1H each, -CH_2-OAc), 2.30, 2.06 (both s, 3H each, 2 x -OCO-CH_3), 1.84 (s, 3H, -CO-CH_3); MS M^+ 426.2035 (calcd. for $C_{25}H_{30}O_6$: 426.2052).

<u>1S*,2S*,3S*,8R*,9R*,10S*)-10-Benzyloxy-2-hydroxy-6-methyl-3-[N,N,N',N'-tetramethylphosphorodiamidoyl]tricyclo-[7.3.0.$0^{3,8}$]dodec-5-ene (87)</u>

A solution of the diol **78** (0.11 g, 0.33 mmole) in tetrahydrofuran (5 mL) was treated with sodium hydride (50% dispersion in mineral oil, 0.021 g, 0.42 mmol) at

0°C. To this mixture was added hexamethylphosphoramide (0.5 mL). The resulting mixture was stirred for 20 min and N,N-dimethylamidophosphorodichloridate (0.5 mL, excess) was added. This slightly turbid mixture was stirred overnight under argon atmosphere at room temperature. The reaction mixture was cooled to 0°C and it was quenched with anhydrous dimethylamine (5.0 mL). The resultant milky white solution was stirred for 3 h at 0°C. The reaction mixture was poured in water and extracted with ether. The ether layer was washed successively with water and saturated brine solution, dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 50% acetone in dichloromethane gave pure monophosphorodiamidate **87** (0.1 g, 68% yield): IR 3360 cm^{-1}; ^1H NMR δ 7.30 (s, 5H, aromatic), 5.39 (bs, 1H, -CH=C-), 4.59, 4.51 (ABq, 1H each, J = 12 Hz, $PhCH_2$-O-), 3.85 (m, 2H, -O-CH- and -CHH-O-PO-), 3.70 (m, 2H, -CH-OH and -CHH-O-PO-), 2.66, 2.68, (both d, 6H each, J = 11 Hz, 2 x $-NMe_2$), 1.68 (bs, 3H, CH_3-C=); carbon-13 NMR δ 139.42, 130.69, 128.27, 127.26, 127.00, 118.21, 83.27, 81.85, 71.83, 68.16, 68.07, 53.93, 45.38, 45.32, 45.20, 45.08, 38.68, 36.59, 34.58, 30.17, 29.32, 26.12, 23.81; MS M^+ 462.2651 (calcd. for $C_{25}H_{39}N_2O_4P$: 462.2647), m/e 417.2068 (M^+-45, calcd. for $C_{23}H_{32}NO_4P$: 417.2071).

(1R*,2R*,7R*,12R*,13R*,14S*)-14-Benzyloxy-4-N,N-dimethylamino-10-methyl-4-oxo-3,5-dioxa-4-phosphatetracyclo[12.3.0.0^{2,7}.0^{7,12}]hexadec-9-ene (90)

Sodium hydride (50% dispersion in mineral oil; 0.6 g, 2.5 mmol) was added to the stirred solution of the diol **81** (0.3 g, 0.92 mmol) in tetrahydrofuran (5 mL) at 0°C. Hexamethylphosphoramide (0.6 mL) was added to this mixture. After stirring for 15 min, N,N-dimethylamidophosphorodichloridate (0.6 mL, excess) was added. The reaction mixture was stirred overnight under argon atmosphere at room temperature. It was cooled to 0°C and was quenched with anhydrous dimethylamine (15.0 mL). The resulting milky white solution was stirred for 3 h. It was poured in water and extracted with ether. The ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 10-30% acetone in dichloromethane, gave pure cyclic phosphoramidate **90** (0.27 g, 70% yield): IR 1250 (P=O), 1000 cm^{-1} (P-O-C); ^{1}H NMR δ 7.30 (s, 5H, aromatic), 5.26 (bs, 1H, C**H**=C-), 4.59, 4.49 (ABq, 1H each, J = 11 Hz, PhC**H**$_2$-O-), 4.53 (d, 1H, J = 6 Hz, -PO-O-C**H**-), 4.32 (dd, 1H, J = 12 Hz, J' = 2 Hz, -C**H**H-O-PO-), 4.05 (dd, 1H, J = 22 Hz, J' = 12 Hz, -CH**H**-O-PO-), 3.93 (m, 1H, -O-C**H**-), 2.69 (d, 6H, J = 11 Hz, -NMe$_2$), 1.66 (bs, 3H,

CH_3-C=C-); MS M^+ 417.2063 (calcd. for $C_{23}H_{32}NO_4P$: 417.2066).

Anal. calcd. for $C_{23}H_{32}NO_4P$: C, 66.18; H, 7.73. Found: C, 65.47; H, 7.88.

(1R*,2R*,3S*,8R*,9R*,10S*)-2,8-Dihydroxy-4,6-dimethyltricyclo[7.3.0.0^{3,8}]dodec-5-ene (**91**)

To anhydrous ethylamine (10 mL), cooled to 0°C, was added lithium (0.35 g, 48 mmol) with stirring. Most of the lithium dissolved within 20-30 min resulting in a very deep blue solution. To it was added a solution of the cyclic phosphoramidate **90** (0.2 g, 0.48 mmol) in tetrahydrofuran (3 mL). After stirring for 3 h at room temperature, under argon atmosphere the reaction was quenched with water and extracted with ether. The combined ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel, eluting with 2% ether in dichloromethane, gave pure diol **91** (0.05 g, 49% yield): IR 3360 cm^{-1}; ^{1}H NMR δ 5.37 (bs, 1H, -CH=C-), 4.00 (m, 1H, -CH_2-CHOH), 3.30 (d, 1H, J = 6 Hz, -CH-CHOH), 1.66 (s, 3H, CH_3-C=C-), 1.06 (s, 3H, CH_3-C-); MS M^+ 222.1623 (calcd. for $C_{14}H_{22}O_2$: 222.1626), m/e 204.1514 (M^+-18; calcd. for

$C_{14}H_{20}O$: 204.1520); m/e 186.1406 (M^+-36; calcd. for $C_{14}H_{18}$: 186.1408).

(1R*,2S*,3R*,8R*,9R*,10S*)-10-Benzyloxy-2-methanesulfonyloxy-3-methanesulfonyloxymethyl-6-methyltricyclo-[7.3.0.0^{3,8}]dodec-5-ene (92)

To a solution of the diol **78** (5.0 g, 15.25 mmol) in dichloromethane (50 mL) was added triethylamine (20 mL). On cooling this solution to 0°C, methanesulfonyl chloride (4.2 g, 2.9 mL, 37 mmol) was added in a drop-wise fashion. The resulting reaction mixture was stirred under argon atmosphere for 30 min. It was poured in water and extracted with ether. The combined ether extract was washed with water, dilute hydrochloric acid, saturated sodium carbonate solution, water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with dichloromethane gave pure dimesylate **92** (5.9 g, 90% yield): IR 1356 and 1175 cm^{-1} (both -O-SO_2-); ^1H NMR δ 7.32 (s, 5H, aromatic), 5.30 (bs, 1H, $\overset{|}{C}H=\overset{|}{C}$-), 4.68 (d, 1H, J = 7 Hz, -$\overset{|}{C}H$-SO_2-), 4.62, 4.47 (ABq, 1H each, J = 12 Hz, PhCH_2-O-) 4.08, 4.06 (both s, 1H each, -CH_2-OSO_2-), 3.84 (m, 1H, -$\overset{|}{C}H$-O-), 3.05, 3.07 (both s, 3H each, -SO_2CH_3), 1.68 (s, 3H, CH_3-$\overset{|}{C}$=$\overset{|}{C}$-); MS M^+

484.1589 (calcd. for $C_{23}H_{32}O_7S_2$: 484.1555), m/e 388.1709 (M^+-96; calcd. for $C_{22}H_{28}O_4S$: 388.1708).

(1R*,2R*,4S*,9R*,10S*,11S*)-11-Benzyloxy-7-methyltetracyclo[8.3.0.$0^{2,4}$.$0^{2,9}$]tridec-6-ene (**93**)

A mixture of the dimesylate **92** (0.5 g, 1 mmol), lithium iodide (1.4 g, 10 mmol) and zinc dust (0.7 g, 10 mmol) in dimethylformamide (10 mL) was heated at 145°C under argon atmosphere for 14 h. After cooling the reaction mixture to room temperature, it was diluted with ether. The solid material was filtered off and washed with ether. The combined ether layer was washed with water and saturated brine solution. It was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 2-10% dichloromethane in hexane, gave pure compound **93** (0.23 g, 75% yield): ^{1}H NMR δ 7.34 (s, 5H, aromatic), 5.46 (bs, 1H, -CH=C-), 4.61, 4.47 (ABq, 1H each, J = 12 Hz each, PhC**H**$_2$-O-), 3.79 (m, 1H, -O-C**H**-), 1.70 (s, 3H, CH_3-C=C-), 1.30 (t, 1H, J = 4 Hz, cyclopropane-C**H**H), 1.24 (ddd, 1H, J = 4 Hz, J' = 5.5 Hz, J" = 8 Hz, cyclopropane-C**H**), 0.16 (dd, 1H, J = 4 Hz, J' = 8 Hz, cyclopropane-CH**H**); MS M^+ 294.1975 (calcd. for $C_{21}H_{26}O$: 294.1984) m/e 203.1420 (M^+-91; calcd. for $C_{14}H_{19}O$: 203.1427).

(1R*,2R*,3R*,8R*,9R*,10S*)-10-Benzyloxy-2-hydroxy-3,6-dimethyltricyclo[7.3.0.0^{3,8}]dodec-5-ene (**96**)

To a solution of the cis-diol **81** (1 g, 3 mmol) in dichloromethane (10 mL), at 0°C, was added triethylamine (10 mL) and methanesulfonyl chloride (0.85 g, 0.6 mL, 7.3 mmol). The resulting mixture was stirred under argon atmosphere for 30 min and poured in water. The aqueous layer was extracted with ether. The ether layer was washed with water, saturated sodium carbonate solution, dilute hydrochloric acid and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. The crude dimesylate thus obtained (1.7 g) was pure enough for further use. It was dissolved in dimethylformamide (20 mL). To this solution was added lithium iodide (3.1 g, 23 mmol) and zinc dust (1.6 g, 25 mmol). The resulting mixture was heated at 145°C under argon atmosphere for 14 h. After cooling it was diluted with ether. The solids were filtered off and washed with ether. The combined filtrate was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 1-4% ether in dichloromethane, gave pure alcohol **96** (0.35 g, 45% yield from **81**): IR 3360 cm^{-1}; ^{1}H NMR δ 7.30 (s, 5H, aromatic), 5.32 (bs, 1H, -CH=C-), 4.66, 4.49 (ABq, 1H

each, J = 12 Hz, $PhCH_2$-O-), 3.80 (m, 1H, -O-CH-), 3.46 (d, 1H, J = 5 Hz, -CH-OH), 1.66 (s, 3H, CH_3C=C-), 1.02 (s, 3H, CH_3-C-); MS M^+ 312.2084 (calcd. for $C_{21}H_{28}O_2$: 312.2089), m/e 294.1971 (M^+-18; calcd. for $C_{21}H_{26}O$: 294.1983).

(1R*,2S*,3S*,8R*,9R*,10S*)-10-Benzyloxy-2-hydroxy-6-methyl-3-phenoxythionocarbonyloxymethyltricyclo-[7.3.0.$0^{3,8}$]dodec-5-ene (**97**)

The trans-diol **78** (8 g, 24 mmol) and 4-(N,N-dimethylamino)pyridine (4 g, 33 mmol) were dissolved in acetonitrile (300 mL). This solution was treated with phenyl chlorothionocarbonate (7 g, 5.4 mL, 39 mmol). The resulting orange-yellow solution was stirred at room temperature under the atmosphere of argon for 60 h. The solvent from the reaction mixture was removed under reduced pressure and the residue was taken up in ether. The ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 1-5% ether in dichloromethane, gave pure compound **97** (6.8 g, 60% yield): IR 3440 cm^{-1}; ^1H NMR δ 7.36 (m, 10H, aromatic), 5.39 (bs, 1H, -CH=C-), 4.62, 4.51 (ABq, 1H each, J = 12.5 Hz, Ph-CH_2-O-), 4.58, 4.28 (ABq, 1H each, J = 11 Hz, -CH_2-O-CS-),

3.84 (m, 1H, -O-CH-), 3.60 (d, 1H, J = 7 Hz, -CHOH), 1.69 (s, 3H, CH_3-C-); carbon-13 NMR δ 194.98, 153.22, 139.15, 131.17, 129.55, 128.27, 127.27, 126.93, 126.56, 121.74, 117.26, 84.31, 81.54, 76.65, 71.81, 46.32, 45.67, 44.94, 35.54, 30.1, 29.23, 26.26, 23.86, 23.67; MS m/e 370.1602 (M^+-94; calcd. for $C_{22}H_{26}O_3S$: 370.1603), m/e 310.1931 (M^+-134; calcd. for $C_{21}H_{26}O_2$: 310.1933).

(1R*,2S*,3R*,8R*,9R*,10S*)-10-Benzyloxy-3,6-dimethyl-2-hydroxytricyclo[7.3.0.$0^{3,8}$]dodec-5-ene (**99**)

The thionocarbonate derivative **97** (6.5 g, 14 mmol), tri-n-butyltin hydride (6.1 g, 5.66 mL, 21 mmol) and 2,2'-azobis(2-methyl-2-propionitrile) (0.1 g) were dissolved in toluene (150 mL). The resulting solution was deaerated by bubbling argon through it for 20 min. The deaerated solution was refluxed under the argon atmosphere for 2.5 h. The color of the solution changed from deep red to almost colorless. The reaction mixture, after cooling to room temperature, was concentrated. Purification by chromatography on silica gel column, eluting with 2-8% ether in dichloromethane, gave pure alcohol **99** (4.3 g, quantitative): IR 3440 cm^{-1}; ^1H NMR δ 7.34 (s, 5H, aromatic), 5.34 (bs, 1H, -CH=C-), 4.58, 4.49 (ABq, 1H each, J = 12 Hz, $PhCH_2$-O-), 3.80 (m, 1H, -O-CH-), 3.30 (d, 1H, J = 7 Hz, -CHOH), 1.66 (s, 3H, CH_3-C=C-), 0.98 (s, 3H, CH_3-C-);

carbon-13 NMR δ 139.34, 130.80, 128.29, 127.26, 127.00, 118.05, 88.89, 81.88, 71.89, 47.21, 45.55, 41.63, 40.04, 30.06, 29.75, 29.33, 28.18, 26.25, 23.86; MS M^+ 312.2081 (calcd. for $C_{21}H_{28}O_2$: 312.2106) m/e 294.1976 (M^+-18; calcd. for $C_{21}H_{26}O$: 294.1984).

Anal. calcd. for $C_{21}H_{28}O_2$: C, 80.77, H, 8.97. Found: C, 80.85; H, 8.77.

(1R*,2R*,7R*,12R*,13R*,14S*)-14-Benzyloxy-10-methyl-4-thiono-3,6-dioxatetracyclo[12.3.0.0.^{2,7}0^{7,12}]hexadec-9-ene (**100**)

A solution of the diol **81** (0.05 g, 0.15 mmol) and 4-(N,N-dimethylamino)pyridine (0.05 g, 0.38 mmol) in acetonitrile (2.0 mL) was treated with pheny chlorothionocarbonate (0.07 g, 0.05 mL, 0.38 mmol) with stirring at room temperature. The resulting light yellow colored solution was stirred at room temperature for 36 h. The reaction mixture was diluted with ether and washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Purification on a silica gel column, eluting with dichloromethane, gave pure cyclic thionocarbonate **100** (0.03 g, 50% yield): IR 1250 cm^{-1} (C=S); ^1H NMR δ 7.30 (s, 5H, aromatic), 5.30 (bs, 1H, -CH=C-), 4.64 and 4.56 (AB quartet, 2H, J = 12 H, each, PhCH_2-O-), 4.00. (d, 1H,

J = 6 Hz, -CH-O-CS-), 4.08, 4.20 (AB quartet, 2H, J = 11 Hz each, $-CH_2-O-CS-$), 3.94 (m, 1H, -O-CH-), 1.70 (s, 1H, $CH_3-C=C-$); MS M^+ 370.1605 (calcd. for $C_{22}H_{26}O$: 370.1602).

(1R*,2R*,3R*,8R*,9R*,10S*)-10-Benzyloxy-3,6-dimethyl-2(N,N,N',N'-tetramethyl)phosphorodiamidoyltricyclo-[7.3.0.0^{3,8}]dodec-5-ene (**101**)

A solution of the alcohol **96** (0.25 g, 0.8 mmol) in tetrahydrofuran (5 mL) at 0°C was treated with sodium hydride (50% dispersion in mineral oil; 0.05 g, 1 mmol) and hexamethylphosphoramide (0.5 mL). After stirring the resulting mixture for 20 min at 0°C, N,N-dimethylamidophosphorodichloridate (0.5 mL, excess) was added. This slightly turbid solution was stirred overnight under argon atmosphere at room temperature. It was cooled to 0°C and quenched with anhydrous dimethylamine (10 mL) and stirred for an additional 3 h. The reaction mixture was poured into water and extracted with ether. The ether extract was washed with water and saturated brine solution. After drying the ether extract over anhydrous sodium sulfate it was concentrated to give crude product. Purification by chromatography on silica gel column, eluting with 50% acetone in dichloromethane, gave pure phosphorodiamidate **101** (0.2 g, 60%): ^{1}H NMR δ 7.34 (s, 5H, aromatic), 5.28 (bs, 1H, -CH=C-), 4.59, 4.49 (ABq, 1H each, J = 14 Hz,

Ph-C**H**$_2$-O-), 4.27 (dd, 1H, J = 6 Hz, J' = 10 Hz, -CH-O-PO-), 2.85, 2.70, (2 x d, 6H, J = 11 Hz, each, 2 x -NMe$_2$), 1.66 (s, 3H, CH_3-C=C-), 1.26 (s, 3H, CH_3-C-); MS M^+ 446.2700 (calcd. for $C_{25}H_{39}N_2O_3P$: 446.2702), m/e 294.1979 (M^+-152; calcd. for $C_{21}H_{26}O$: 294.1983).

(1R*,2S*,3R*,8R*,9R*,10S*)-10-Benzyloxy-3,6-dimethyl-2(N,N,N',N'-tetramethyl)phosphorodiamidoyltricyclo-[7.3.0.0^{3,8}]dodec-5-ene (**102**)

A solution of alcohol **99** (0.1 g, 0.3 mmol) in tetrahydrofuran (3 mL) at 0°C was treated with sodium hydride (50% dispersion in oil; 0.01 g, 0.4 mmol) and hexamethylphosphoramide (0.2 mL). This solution was stirred for 15 min and N,N-dimethylamidophosphorodichloridate (0.2 mL, excess) was added. The resulting reaction mixture was stirred overnight under the atmosphere of argon. It was cooled to 0°C and quenched with anhydrous dimethylamine (5 mL) and the milky white solution thus formed was stirred for 3 h. The reaction mixture was poured into water and extracted with ether. The ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography of the residue on silica gel column, eluting with 50% acetone in dichloromethane, gave pure compound **102** (0.8 g, 56%

yield): IR 1225 cm^{-1} (P = O): ^1H NMR δ 7.30 (s, 5H, aromatic), 5.33 (bs, 1H, -CH=C-), 4.58, 4.47 (ABq, 1H each, J = 12.5 Hz, $PhCH_2$-O-), 3.98 (dd, 1H, J = 7 Hz, J' = 7 Hz, -CH-OPO-), 3.80 (m, 1H, -O-CH-), 2.72, 2.70, (2 x d, 6H each, J = 11 Hz, $2xNMe_2$), 1.66 (s, 3H, CH_3-C=C-), 0.99 (s, 3H, CH_3-C-); carbon-13 NMR δ 139.27, 130.62, 128.31, 127.17, 126.92, 117.83, 113.01, 112.81, 91.14, 91.01, 81.75, 71.73, 45.77, 45.41, 42.11, 39.39, 36.57, 36.51, 29.63, 29.10, 28.96, 25.80, 23.72, 22.74; MS M^+ 446.2702 (calcd. for $C_{25}H_{39}N_2O_3P$: 446.2699), m/e 294.1986 (M^+-152; calcd. for $C_{21}H_{26}O$: 294.1983).

1S*,3R*,8R*,9S*,10S*)-10-Hydroxy-3,6-dimethyltricyclo-[7.3.0.$0^{3,8}$]dodec-5-ene (**103**)

a) From the phosphorodiamidate **101**.

Pieces of lithium (0.25 g, 34 mmol) were added to ethylamine (10 mL) cooled to 0°C. Within 20-30 min most of the pieces dissolved resulting in a very deep blue solution. To this solution was added the phosphorodiamidate **101** (0.15 g, 0.34 mmol) in tetrahydrofuran (5 mL). The resulting mixture was stirred at room temperature under the argon atmosphere overnight. The reaction mixture was quenched with water and extracted with ether. The ether layer was washed with water and saturated brine

solution. It was dried over anhydrous sodium sulfate and concentrated. Purification by chromatography on silica gel column, eluting with 2-5% ether in dichloromethane, gave pure alcohol **103** (0.035 g, 50%): IR 3380 cm^{-1}; ^1H NMR δ 5.30 (bs, 1H, -CH=C-), 4.20 (m, 1H, -CHOH), 1.66 (s, 3H, CH_3-C=C-), 0.98 (s, 3H, CH_3-C); MS M^+ 206.1662 (calcd. for $C_{14}H_{22}O$: 206.1670), m/e 188.1558 (M^+-18; calcd. for $C_{14}H_{20}$: 188.1565).

b) From the phosphorodiamidate **102**

Pieces of lithium (0.13 g, 17 mmol) were added to ethylamine (10 mL) cooled to 0°C. Within 20-30 min, most of the pieces dissolved giving a very deep blue solution. To this solution was added the phosphorodiamidate **102** (0.7 g, 0.17 mmol) in tetrahydrofuran (5 mL). The resulting solution was stirred at room temperature overnight under the atmosphere of argon. The reaction mixture was quenched with water and extracted with ether. The combined ether extract was washed with water and saturated brine solution. It was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 2-5% ether in dichloromethane, gave alcohol **103** (0.018 g, 50%).

(1R*,2S*,3R*,8R*,9R*,10S*)-10-Benzyloxy-3,6-dimethyl-2-methanesulfonyloxytricyclo[7.3.0.0^{3,8}]dodec-5-ene (**104**)

The alcohol **99** (2 g, 6.4 mmol) was dissolved in a 1:1 mixture of dichloromethane (10 mL) and triethylamine (10 mL) and cooled to 0°C. Methanesulfonyl chloride (1 g, 0.7 mL, 8.7 mmol) was added and the resulting brown reaction mixture was stirred under the atmosphere of argon for 30 min at room temperature. The reaction mixture was poured into water and extracted with ether. The combined ether extract was washed with water, saturated sodium carbonate solution, dilute hydrochloric acid and saturated brine solution. It was dried over anhydrous sodium sulfate and concentrated. Purification by chrmatography on silica gel column, eluting with dichloromethane, gave pure mesylate **104** (2.2 g, 90%): IR 1351 and 1173 cm^{-1} ($-SO_2-O-$); ^1H NMR δ 7.34 (s, 5H, aromatic), 5.33 (bs, 1H, -CH=C-), 4.59, 4.48 (ABq, 1H each, J = 12.5 Hz, $PhCH_2-O-$), 4.33 (d, 1H, J = 7 Hz, $-CHOSO_2-$), 3.82 (m, 1H, -OCH-), 3.04 (s, 3H, $-O-SO_2-CH_3$), 1.68 (s, 3H, $CH_3-C=C-$), 1.03 (s, 3H, CH_3-C-); MS M^+ 390.1837 (calcd. for $C_{22}H_{30}O_4S$: 390.1865), m/e 294.1983 (M^+-98; calcd. for $C_{21}H_{26}O$: 294.1984).

(1S*,3R*,8R*,9S*,10S*)-10-Benzyloxy-3,6-dimethyltricyclo-[7.3.0.0^{3,8}]dodec-5-ene (82) and (3S*,8R*,9R*,10S*)-10-Benzyloxy-3,6-dimethyltricyclo[7.3.0.0^{3,8}]dedec-1,5-diene (105)

The mesylate **104** (2 g, 5.1 mmol), lithium iodide (7 g, 52 mmol) and zinc dust (3.5 g, 54 mmol) were placed in dimethylformamide (50 mL). This mixture was heated under the argon atmosphere at 145°C for 14 h. On cooling to room temperature, it was diluted with ether (50 mL) and filtered. The precipitated solids were washed with ether. The filtrate was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatograph of the residue on silica gel column, eluting with 2-5% dichloromethane in hexane, gave pure compound **82** (0.55 g, 36% yield): ^{1}H NMR δ 7.28 (s, 5H, aromatic), 5.28 (bs, 1H, -CH=C-), 4.60, 4.51 (ABq, 1H each, J = 12 Hz, Ph-C**H**$_2$-O-), 3.82 (m, 1H, -O-CH-), 1.66 (d, 3H, J = 3.5 Hz, CH_3-C=C-) 0.98 (s, 3H, CH_3-C-); carbon-13 NMR δ 170.26, 139.58, 130.52, 128.27, 127.17, 127.00, 118.98, 82.51, 71.88, 49.59, 48.98, 43.67, 39.85, 38.58, 33.57, 30.26, 28.84, 28.11, 25.14, 23.88; MS M^+ 296.2136 (calcd. for $C_{21}H_{28}O$: 296.2140).

Anal. calcd. for $C_{21}H_{28}O$: C, 85.14; H, 9.46. Found: C, 85.37; H, 9.63.

Continued elution of the column with 8-10% dichloromethane in hexane gave compound **105** (0.3 g, 20% yield): ^1H NMR δ 7.34 (s, 5H, aromatic), 5.50 (bs, 1H, -CH=C(-)-CH_3), 5.38 (s, 1H, -CH=C(-)-), 4.62, 4.50 (ABq, 1H each, J = 12 Hz, Ph-CH_2-O-), 3.80 (t, 1H, J = 6 Hz, -O-CH(-)-), 1.70 (s, 3H, CH_3-C(-)=C(-)-), 1.10 (s, 3H, CH_3-C(-)-); carbon-13 NMR δ 148.84, 139.36, 131.91, 131.13, 128.20, 127.40, 127.17, 120.99, 77.30, 70.70, 61.69, 49.89, 43.93, 36.33, 34.89, 30.62, 26.48, 23.72, 21.96; MS M^+ 294.1984 (calcd. for $C_{21}H_{26}O$: 294.1984).

(1R*,2S*,3R*,8R*,9R*,10S*)-10-Benzyloxy-3,6-dimethyl-2-methylmecaptothionocarbonyloxytricyclo[7.3.0.$0^{3,8}$]dodec-5-ene (**106**)

A solution of the alcohol **99** (2 g, 6.4 mmol) in tetrahydrofuran (25 mL) at 0°C was treated with potassium hydride (35% dispersion in mineral oil; 1 g, 7.7 mmol). After stirring for 20 min, this solution was treated with carbon disulfide (1.8 g, 1.4 mL, 24 mmol). The resulting deep brown solution was stirred under the argon atmosphere at room temperature for 16 h. To this reaction mixture was added methyl iodide (4.6 g, 2 mL, 32 mmol). The resulting light brown solution was stirred further for 12 h under the atmosphere of argon at room temperature. The solvent was removed under reduced pressure and the residue

was taken up in ether. The ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 5-20% dichloromethane in hexane, gave pure compound **106** (1 g, 40% yield): IR 1052 cm^{-1} (C=S); ^1H NMR δ 7.34 (s, 5H, aromatic), 5.69 (d, 1H, J = 7 Hz, -CH-OCS-), 5.34 (bs, 1H, -CH=C-), 4.60, 4.48 (ABq, 1H each, J = 12 Hz, $PhCH_2$-O-), 3.82 (m, 1H, -O-CH-), 2.66 (s, 3H, -S-CH_3), 1.66 (s, 3H, CH_3-C=C-), 0.96 (s, 3H, CH_3-C-); CIMS ($M+NH_4^+$) 420.00; MS m/e 355.1739 (M^+-47; calcd. for $C_{22}H_{17}O_2S$: 355.1732), m/e 294.1985 (M^+-108; calcd. for $C_{21}H_{26}O$: 294.1983).

(1S*,3R*,8R*,9S*,10S*)-10-Benzyloxy-3,6-dimethyltricyclo-[7.3.0.$0^{3,8}$]dodec-5-ene (**82**) from Xanthate **106**

The xanthate **106** (1 g, 2.5 mmol), tri-n-butyltin hydride (2.5 g, 2.3 mL, 8.6 mmol) and 2,2'-azobis(2-methyl-2-propionitrile) (0.1 g) were dissolved in toluene (20 mL). The solution was deaerated by bubbling argon gas for 20 min. This solution was refluxed under the argon atmosphere for 2 h. The reaction mixture was cooled to room temperature and concentrated. The residue on chromatography on silica gel column, eluting with 2-6% dichloromethane in hexane, gave pure **82** (0.73 g, quantitative).

(1S*,3S*,7S*,8S*,9S*)-6-Acetyl-9-benzyloxy-3-methyltricyclo-[6.3.0.$0^{3,7}$]undec-5-ene (**107**)

The benzyl ether **82** (0.5 g, 1.6 mmol) was dissolved in dichloromethane (15 mL). The solution was cooled to -78°C and ozone was passed through the solution till the blue color of ozone persisted. The flow of ozone was stopped, the solution was purged with argon to remove excess ozone and dimethyl sulfide (5 mL) was added. The resulting solution was stirred overnight under the argon atmosphere allowing the temperature to rise to the room temperature. The reaction mixture was concentrated and the residue was taken up in ether. The ether layer was washed with water and saturated brine solution, dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with dichloromethane, gave pure enone **107** (0.32 g, 60% yield): IR 1660 (C=O), 1614 cm^{-1} (C=C); ^1H NMR δ 7.42-7.24 (m, 5H, aromatic), 6.69 (t, 1H, J = 2.5 Hz, -CH=C-), 4.68, 4.58 (ABq, 1H each, J = 12 Hz, $PhCH_2$-O-), 3.98 (m, 1H, -O-CH-), 3.22 (bs, 1H, -CH-C=CH-), 2.32 (s, 1H, CH_3-CO-), 1.12 (s, 3H, CH_3-C-); carbon-13 NMR δ 148.95, 142.28, 139.76, 128.07, 127.17, 126.92, 81.98, 71.25, 57.35, 54.48, 53.30, 48.45, 47.72, 43.97, 32.71, 28.66, 27.25, 26.78; MS M^+ 310.1932 (calcd. for $C_{21}H_{26}O_2$: 310.1933).

(1S*,3S*,7S*,8S*,9S*)-9-Benzyloxy-6-carbomethoxy-3-methyltricyclo[6.3.0.0^{3,7}]undec-5-ene (**110**)

Sodium methoxide was generated by dissolving sodium (0.08 g) in methanol (5 mL). The resulting sodium methoxide solution was cooled to 0°C and iodine (0.16 g, 1.25 mmol) was added to it. After stirring this mixture for 20 min, a solution of enone **107** (0.1 g, 0.33 mmol) in methanol (3.0 mL) was added and stirring, under the atmosphere of argon, was continued for additional 30 min. The reaction mixture was diluted with water and extracted with ether. The ether layer was washed with a dilute solution of sodium thiosulfate, water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with dichloromethane, gave pure ester **110** (0.05 g, 45% yield): IR 1717 (ester C=O), 1620 cm^{-1} (C=C); ^{1}H NMR δ 7.38-7.28 (m, 5H, aromatic), 6.62 (bs, 1H, -CH=C-CO-), 4.65, 4.52 (ABq, 1H each, J = 12 Hz, PhC**H**$_2$-O-), 3.92 (m, 1H, -O-CH-), 3.78 (s, 3H, -COOCH$_3$), 3.20 (bs, 1H, -C**H**-C=CH-), 1.12 (s, 3H, CH$_3$-C-); MS M$^+$ 326.1885 (calcd. for $C_{21}H_{26}O_3$: 326.1882).

(1S*,3S*,7S*,8S*,9S*)-9-Benzyloxy-6-carboethoxymethylidene-3-methyltricyclo[6.3.0.0^{3,7}]undeca-5-ene (**115**)

To the saturated solution of chlorine gas in di-

chloromethane (3.0 mL) at 0°C was added the enone **107** (0.02 g, 0.065 mmol). The resulting solution was stirred for 10 min and the solvent was removed under reduced pressure. The residue was redissolved in ethanol (5.0 mL) containing sodium ethoxide (0.05 g) and refluxed under argon atmosphere for 2 h. The reaction mixture was diluted with water and extracted with ether. The ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with dichloromethane, gave pure **115** (0.006 g, 25% yield): IR 1711 cm^{-1} (C=O); ^1H NMR δ 7.34-7.40 (m, 5H, aromatic), 5.58 (bs, 1H, -CH=CO-), 4.60, 4.54 (ABq, 1H each, J = 12 Hz, $PhC\mathbf{H}_2$-O-), 4.15 (q, 2H, J = 7 Hz, CH_3-$C\mathbf{H}_2$-O-CO-), 3.84 (m, 1H, -O-CH-), 1.28 (t, 3H, J = 7 Hz, $C\mathbf{H}_3$-CH_2-O-CO-), 1.00 (s, 3H, CH_3-C-); MS M^+ 354.2184 (calcd. for $C_{23}H_{30}O_3$: 354.2195).

(1S*,3S*,7S*,8S*,9S*)-9-Benzyloxy-3-methyltricyclo-[6.3.0.$0^{3,7}$]undecan-6-one (117)

The enone **107** (0.2 g, 0.65 mmol) and fused sodium acetate (0.5 g) were placed in methanol (5 mL). To this suspension was added hydroxylamine hydrochloride (0.06 g, 0.78 mmol) and the resulting mixture was stirred for 2.5 h at room temperature. The reaction mixture was taken up in

ether and washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated.

The oxime **118** (0.3 g) thus obtained was dissolved in a 1:1 mixture of pyridine (3 mL) and triethylamine (3 mL). The solution was cooled to -23°C and phosphorous oxychloride (0.5 mL, excess) was dripped into the reaction mixture. The resulting deep red solution was stirred overnight under the atmosphere of argon at 0°C. The reaction mixture was cooled to -15°C and water (10 mL) was added. On stirring this mixture for 15 min, aqueous hydrochloric acid (6 N, 15 mL) was added. Stirring was continued further for 3 h at room temperature. The reaction mixture was extracted with ether and the ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with dichloromethane, gave pure ketone **117** (0.125 g, 70% yield): IR 1725 cm^{-1} (C=O); ^1H NMR δ 7.40-7.28 (m, 5H, aromatic), 4.65, 4.49 (ABq, 1H each, J = 12 Hz, $PhCH_2$-O-), 3.89 (m, 1H, -O-$\overset{|}{C}$H-), 1.18 (s, 3H, CH_3-$\overset{|}{C}$-); MS M^+ 284.1773 (calcd. for $C_{19}H_{24}O_2$: 284.1777).

Anal. calcd. for $C_{19}H_{24}O_2$: C, 80.28; H, 8.45. Found: C, 80.51; H, 8.54.

(1S*,3S*,7S*,8S*,9S*)-9-Benzyloxy-3-methyl-6-methylidenetricyclo[6.3.0.$0^{3,7}$]undecane (**119**)

To a stirred suspension of methyltriphenylphosphonium bromide (0.38 g, 1 mmol) in benzene was added potassium t-butoxide (0.125 g, 1.1 mmol). The resulting suspension was stirred at room temperature under the argon atmosphere for 20 min. The ketone **117** (0.2 g, 0.7 mmol) was added to this bright yellow suspension. The resulting solution was refluxed overnight under the atmosphere of argon. On cooling to room temperature, the reaction mixture was poured in water and extracted with ether. The combined ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column. eluting with 5-20% dichloromethane in hexane, gave pure compound **119** (0.16 g, 80% yield): IR 1650, 880 cm^{-1} (-C(-)=CH_2); ^1H NMR δ 7.38-7.26 (m, 5H, aromatic), 4.88 (bs, 1H, -C(-)=CHH), 4.82 (m, 1H, -C(-)=CHH), 4.58 (s, 2H, $PhCH_2$-O-), 3.85 (m, 1H, -O-CH(-)-), 1.06 (s, 3H, CH_3-C(-)-); MS M^+ 282.1974 (calcd. for $C_{20}H_{26}O$: 282.1983).

(1S*,3S*,7R*,8S*,9S*)-9-Benzyloxy-3-methylspiro[tricyclo-[6.3.0.$0^{3,7}$]undecane[6,1']cyclopropane] (**120**)

The compound **119** (0.15 g, 0.53 mmol) was dissolved in toluene (5 mL). To this was added diethyl zinc (15% (W/V)

solution in toluene; 1.75 mL, 2.1 mmol) and methylene iodide (0.6 g, 0.18 mL, 2.25 mmol). This mixture was stirred at room temperature under the argon atmosphere for few minutes. Argon flow was replaced by a gentle stream of air and the mixture was heated at 50°C for 2 h. The reaction mixture was cooled to room temperature. It was poured into water and extracted with ether. The ether layer was washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 5-15% dichloromethane in hexane, gave pure compound **120** (0.13 g, 80% yield): ^{1}H NMR δ 7.32 (s, 5H, aromatic), 4.57, 4.42 (ABq, 1H each, J = 12 Hz, $PhCH_2$-O-), 3.77 (m, 1H, J = 6 Hz, -O-CH-), 1.20 (s, 3H, CH_3-C-), 0.55 (m, 2H, cyclopropane CH_2), 0.35 (m, 2H, cyclopropane CH_2); MS m/e 205.1589 (M^+-91; calcd. for $C_{14}H_{21}O$: 205.1593).

(1S*,3S*,7R*,8S*,9S*)-9-Hydroxy-3-methylspiro[tricyclo-[6.3.0.0^{3,7}]undecane[6.1']cyclopropane] (**121**)

The cyclopropane **120** (0.1 g, 0.34 mmol), fused sodium acetate (0.2 g) and 5% Pd-C (0.1 g) were placed in glacial acetic acid (5 mL). This mixture was shaken under the atmosphere of hydrogen (30 psi) at room temperature for 12 h. The reaction mixture was filtered, the residue washed with ether. The filtrate was washed with water,

saturated sodium carbonate solution and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 40% dichloromethane in hexane, gave pure alcohol **115** (0.07 g, quantitative yield): IR 3410 cm^{-1}; ^1H NMR δ 4.08 (m, 1H, -C**H**OH), 1.24 (s, 3H, CH_3-C<), 0.60-0.32 (m, 4H, cyclopropane C**H**$_2$-C**H**$_2$); MS M^+ 206.1661 (calcd. for $C_{14}H_{22}O$: 206.1671), m/e 188.1565 (M^+-18; calcd. for $C_{14}H_{20}$: 188.1565).

(1S*,3S*,7R*,8S*,9S*)-9-Cyclohexylmethoxy-3-methyl-spiro[tricyclo[6.3.0.0^{3,7}]undecane[6,1']cyclopropane] (**122**)

The cyclopropane **120** (0.05 g, 0.17 mmol), fused sodium acetate (0.1 g) and platinum oxide (0.05 g) were placed in glacial acetic acid (5 mL). The mixture was shaken under the atmosphere of hydrogen (30 psi) at room temperature for 12 h. The reaction mixture was filtered and the residue was washed with ether. The filtrate was washed with water, saturated sodium carbonate solution and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 10% dichloromethane in hexane, gave pure compound **122** (0.05 g, quantitative yield): ^1H NMR δ 3.56 (m, 1H, -O-C**H**-), 3.22, 3.07 (both

dd, 1H each, J = 6 Hz each, J' = 9 Hz each, -CH-CH$_2$-O-), 1.20 (s, 3H, CH$_3$-C-), 0.57, 0.50, 0.36, 0.20 (4 x ddd, 1H each, J = 3.5 Hz each, J' = 5.5 Hz each, J" = 8.5 Hz each, 4 x cyclopropane -CHH-); MS M$^+$ 302.2631 (calcd. for $C_{21}H_{34}O$: 302.2652).

(1S*,3S*,7R*,8S*,9S*)-3,6,6-Trimethyltricyclo[6.3.0.0^{3,7}]-undecan-9-ol (**123**)

The alcohol **121** (0.05 g, 0.24 mmol), fused sodium acetate (0.1 g) and platinum oxide (0.1 g) were placed in glacial acetic acid (5 mL). This mixture was shaken under the atmosphere of hydrogen (30 psi) at room temperature for 12 h. The reaction mixture was filtered and the residue was washed with ether. The filtrate was washed with water, saturated sodium carbonate solution and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 50% dichloromethane in hexane, gave pure alcohol **123** (0.05 g, quantitative yield): IR 3410 cm^{-1}; ^{1}H NMR δ 4.12 (m, 1H, -CHOH), 1.22, 1.06, 0.98 (3 x s, 3H each, 3 x -CH$_3$); MS M$^+$ 208.1827 (calcd. for $C_{14}H_{24}O$: 208.1827), m/e 190.1724 (M$^+$-18; calcd. for $C_{14}H_{22}$: 190.1722).

(1S*,3S*,7S*,8S*)-3,6,6-Trimethyltricyclo[6.3.0.0^{3,7}]-undecan-9-one (**13**)

The alcohol **123** (0.02 g, 0.085 mmol) was dissolved in dichloromethane (2 mL) and was treated at room temperature with pyridinium chlorochromate (0.06 g, 0.14 mmol). The resulting dark orange solution was stirred at room temperature for 3 h. The reaction mixture was filtered through a short column of fluorosil. The filtrate was concentrated and the residue was chromatographed on silica gel column eluting with dichloromethane. The pure ketone **13** thus obtained (0.015 g, 80% yield) showed: IR 1737 cm^{-1} (C=O); ^1H NMR δ 1.10, 1.06, 0.96 (3 x s, 3H each, 3 x $-CH_3$); carbon-13 NMR δ 222.40, 64.61, 57.34, 53.22, 48.02, 42.51, 42.30, 41.86, 40.31, 35.12, 30.91, 30.45, 26.15, 24.26; MS M^+ 206.1670 (calcd. for $C_{14}H_{22}O$: 206.1670).

$\Delta^{9(12)}$-Capnellene (**2**)

To a stirred suspension of methyltriphenylphosphonium bromide (0.1 g, 0.03 mmol) in benzene (3 mL) was added potassium t-butoxide (0.04 g, 0.03 mmol). This suspension was stirred for 20 min at room temperature. To the resulting bright yellow solution was added the ketone **13** (0.01 g, 0.05 mmol) and the mixture was refluxed under the atmosphere of argon for 6 h. After cooling the reaction mixture to room temperature, it was taken up in ether and

washed with water and saturated brine solution. The ether layer was dried over anhydrous sodium sulfate and concentrated. Chromatography on silica gel column, eluting with 5-10% dichloromethane in hexane, gave pure compound **2** (0.0075 g, 75% yield): IR 870 cm^{-1} ($C=CH_2$); ^1H NMR δ 4.90 (bs, 1H, $-\overset{|}{C}=CH\mathbf{H}$), 4.80 (bs, 1H, $-\overset{|}{C}=C\mathbf{H}H$), 1.16, 1.06, 0.98 (3 x s, 3H each, 3 x $-CH_3$); carbon-13 NMR δ 159.00, 104.99, 69.16, 53.34, 52.34, 48.00, 46.05, 41.73, 40.62, 31.84, 31.60, 30.85, 29.13, 26.09; MS M^+ 204.1867 (calcd. for $C_{15}H_{24}$: 204.1878).

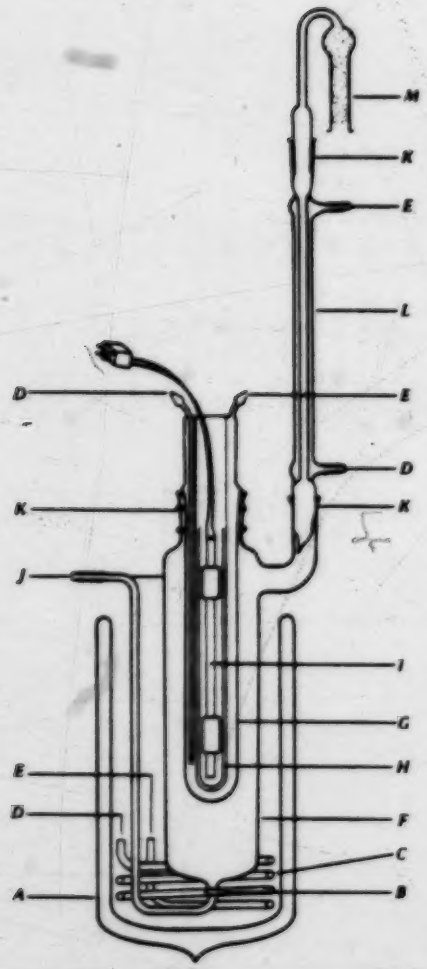

Figure 1. *A*, Dewar flask; *B*, sintered glass filter; *C*, metal cooling coil; *D*, water inlet; *E*, water outlet; *F*, reaction vessel; *G*, quartz immersion well; *H*, pyrex filter; *I*, lamp; *J*, nitrogen gas inlet; *K*, ground glass joint; *L*, condenser; *M*, calcium chloride drying tube.

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